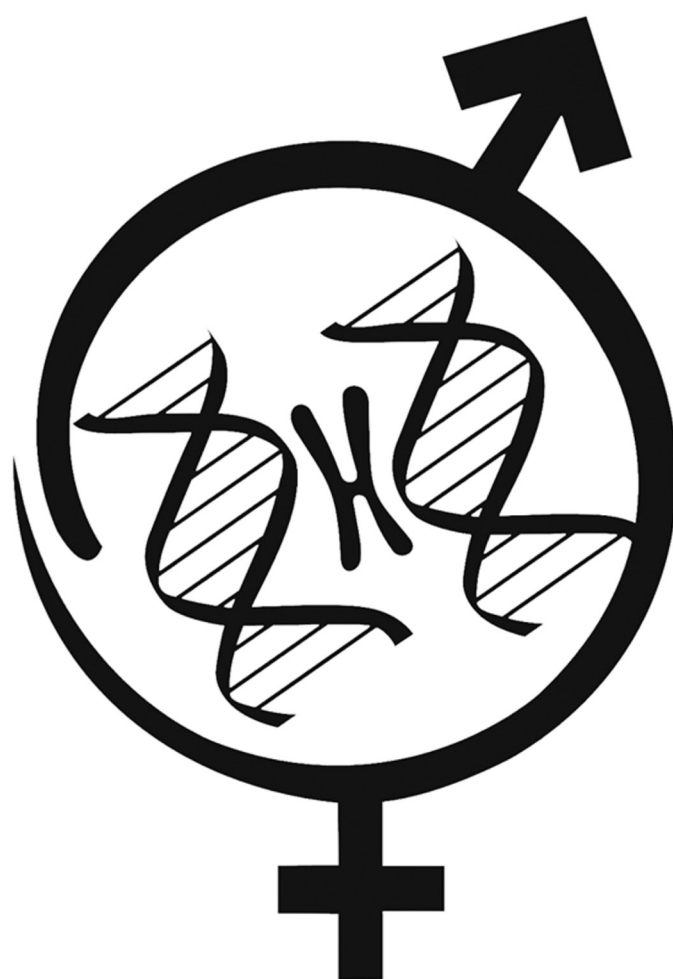


Abstracts of
Royan International Hybrid Twin Congress

26th Hybrid Congress on Reproductive Biomedicine
3-5 September 2025

20th Seminar on Nursing and Midwifery
3-4 September 2025



Royan Institute

Reproductive Biomedicine Research Center
Tehran, Islamic Republic of Iran



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Faramarz Farrahi

Esteemed colleagues,

It is with considerable pleasure that I extend a warm welcome on behalf of the Organizing Committee to the **26th Royan International Congress on Reproductive Biomedicine, convened in Tehran, Iran, from September 3rd to 5th, 2025**. This congress serves as a vital forum for academic scientists, clinicians, and researchers to engage in discourse regarding the latest advancements across diverse facets of reproductive health, encompassing both male and female infertility, clinical embryology, and reproductive genetics.

The program is meticulously structured to incorporate plenary and panel sessions featuring distinguished invited speakers, alongside opportunities for oral and poster presentations, and pre-congress workshops. The discussions will address salient issues within the field of infertility, fostering the adoption of innovative methodologies to enhance our understanding of assisted reproductive techniques and to establish optimal clinical management practices. The congress anticipates the participation of more than 1500 delegates. Continuing in a hybrid modality, the event will feature both in-person and online sessions and presentations, ensuring accessibility for a global audience. This year, the congress received 360 abstracts, marking a significant surge compared to 2024 and underscoring the escalating scientific activity within the realm of Reproductive Biomedicine. The presence of 22 international speakers from 16 countries, coupled with 4 keynote speeches by experienced Iranian and international professors, promises an enriching and informative experience for all attendees. We trust that your engagement with the congress will prove both beneficial and stimulating.

Best regards,

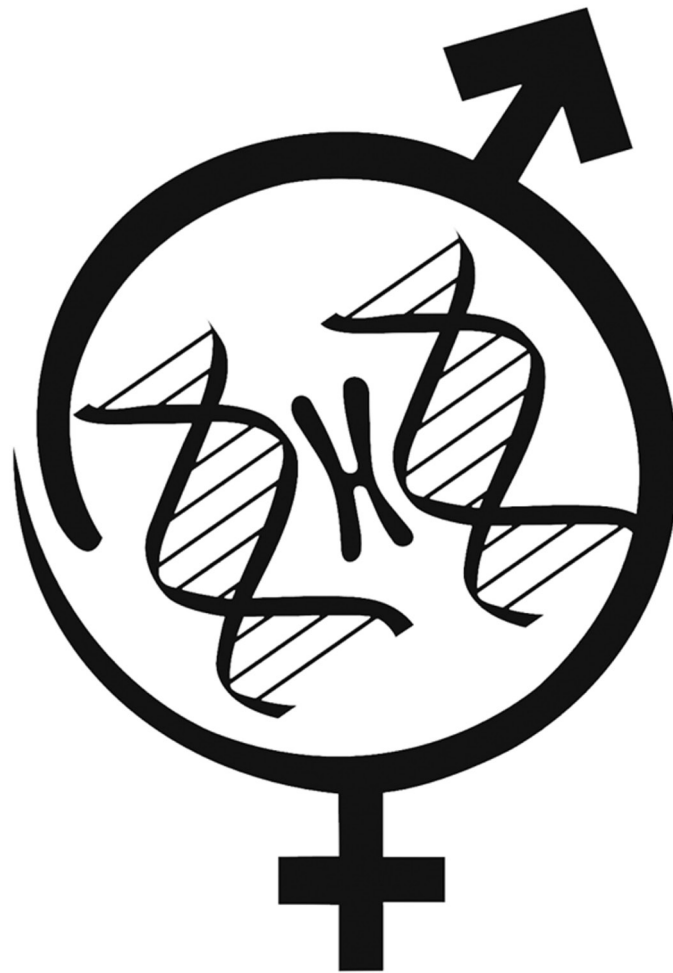
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26th ROYAN International Congress on Reproductive Biomedicine, 2025

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Royan Institute

Reproductive Biomedicine Research Center
Tehran, Islamic Republic of Iran

Invited Speakers

Andrology

I-1: AI-Powered Solutions for Male Infertility

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Background: Male infertility is a rising global health issue, with sperm counts declining by over 50% in the last 50 years. Today, male factors contribute to infertility in over half of all cases, with non-obstructive azoospermia (NOA)—the complete absence of sperm in the ejaculate due to testicular failure—being the most severe form. NOA affects up to 20% of infertile men and poses a significant clinical challenge. The current gold-standard treatment, microdissection testicular sperm extraction (mTESE), requires embryologists to manually search testicular tissue under a microscope for hours to locate rare sperm cells. This process is inefficient, error-prone, and mentally taxing, often leading to missed sperm and inaccurate diagnoses. To address this critical bottleneck in male infertility care, this study investigates the use of an assistive AI tool based on a neural network (CNN) to automate and enhance sperm detection in real time. The system integrates with standard ICSI microscopes to support embryologists by identifying spermatozoa in complex tissue suspensions instantly. By improving speed, accuracy, and throughput, this AI-assisted approach aims to transform the clinical workflow for NOA patients and offer a scalable solution to a growing global reproductive health burden.

Materials and Methods: This two-phase proof-of-concept study began with a training phase using eight azoospermic patients (>10,000 sperm images) to provide a variety of surgically collected samples for sperm morphology and debris variation to train a convolutional neural network to identify spermatozoa. Second, side-by-side testing was undertaken on two cohorts of non-obstructive azoospermia patient samples: an embryologist versus the AI identifying all the spermatozoa in the still images (cohort 1, $n = 4$), and a side-by-side test with a simulated clinical deployment of the AI model with an intracytoplasmic sperm injection microscope and the embryologist performing a search with and without the aid of the AI (cohort 2, $n = 4$).

Results: In cohort 1, the AI model showed an improvement in the time taken to identify all the spermatozoa per field of view ($0.02 \pm 0.30 \times 10^{-5}$ s versus 36.10 ± 1.18 s, $P < 0.0001$) and improved recall ($91.95 \pm 0.81\%$ versus $86.52 \pm 1.34\%$, $P < 0.001$) compared with an embryologist. From a total of 2660 spermatozoa to find in all the samples combined, 1937 were found by an embryologist and 1997 were found by the AI in less than 1000th of the time. In cohort 2, the AI-aided embryologist took significantly less time per droplet (98.90 ± 3.19 s versus 168.7 ± 7.84 s, $P < 0.0001$) and found 1396 spermatozoa, while 1274 were found without AI, although no significant difference was observed.

Conclusion: AI-powered image analysis has the potential for seamless integration into laboratory workflows, to reduce the time to identify and isolate spermatozoa from surgical sperm samples from hours to minutes, thus increasing success rates from these treatments.

Keywords: Azoospermia, Male Infertility, Microdissection Tes-

ticular Sperm Extraction, Spermatozoa, Surgical Sperm Collection

I-2: Sperm DNA Fragmentation and Oxidative Stress

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There are upper limits of assisted reproduction treatment's success. If we look carefully to the results exhibited by all ART programs, we may find two similar patterns among them: first, often a couple needs several attempts to get a child. Second, not every patient succeeds, that lead us to conclude that there is sufficient room for improvement. In some cycles, there may be no embryos to transfer or they are unable to implant. Another subsequent cycle ends up in a child, even when using the same gamete's combination. Same gamete providers-different cycles-different results. This, together with the fact that in an ART procedure, gametes are provided by the patients and afterwards the laboratory intervenes in sperm preparation and selection, lead us to wonder how much this intervention also affects the reproductive performance of a couple. The basic sperm analysis has limited predictive value in the achievement of success in either natural or assisted conception, in part because several non-measured molecular factors within the sperm cells are crucial to succeed. This implies that we have no tools to properly define the probabilities of a sperm sample to successfully accomplish its reproductive function. Several molecular factors have been to some extent related to reproductive outcomes, being sperm DNA fragmentation and oxidative stress two of the most deeply studied, although the vast amount of literature available seem just to confound instead of clarifying the role of sperm DNA integrity and oxidative stress on reproductive success. Oxidative stress and sperm DNA fragmentation seem to closely interact to diminish male reproductive potential, and to some studies, are strong negative indicators for fertilization, embryo development, implantation, miscarriage risk, and live birth rates, while others not. In this lecture, we will provide solid up to date summary, evidence based of the correlation between sperm DNA integrity and oxidative stress with reproductive outcomes, and recommendations about their proper clinical use.

I-3: Dietary Influences on Sperm DNA Integrity: Mechanisms, Evidence, and Clinical Implications

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Male infertility contributes significantly to the approximately 17.5% of couples worldwide experiencing conception difficulties, with sperm DNA fragmentation (SDF) emerging as a crucial biomarker beyond conventional semen analysis. This review comprehensively examines how dietary patterns influence SDF through multifaceted biological mechanisms. Mediterranean and plant-pescatarian diets, characterized by abundant an-

tioxidants, omega-3 fatty acids, and high-quality carbohydrates, demonstrate protective effects by enhancing seminal antioxidant capacity and reducing oxidative damage. These diets align with favorable scores on the Carbohydrate Quality Index (CQI) and Low-Carbohydrate Diet Score (LCDS), which incorporate critical factors like fiber content, whole grain intake, and solid-to-liquid carbohydrate ratios. Conversely, Western and ultra-processed dietary patterns, rich in refined carbohydrates, saturated fats, and processed meats, exacerbate SDF through multiple pathways: promoting lipid peroxidation, increasing postprandial hyperglycemia-induced oxidative stress, and impairing DNA repair mechanisms. At the molecular level, key nutrients including zinc, selenium, and folate from whole food sources contribute to genomic stability by supporting DNA repair enzymes, maintaining proper methylation patterns, and modulating inflammatory cascades. Clinical evidence supports targeted nutritional interventions, with omega-3 supplementation and combined antioxidant therapy showing particular promise in improving sperm chromatin integrity. The review highlights the potential of dietary assessment and personalized nutrition strategies in clinical fertility management, while identifying critical research gaps in understanding gene-nutrient interactions and developing standardized dietary protocols for male reproductive health. These findings underscore the importance of considering dietary factors as both preventive and therapeutic approaches in managing idiopathic male infertility, particularly in cases where conventional semen parameters appear normal yet DNA fragmentation is elevated.

Keywords: Sperm DNA Fragmentation, Male Infertility, Dietary Patterns, Oxidative Stress, Nutritional Interventions, Mediterranean Diet, Carbohydrate Quality Index

I-4: Indications and Optimal Treatment of Distal Ejaculatory Duct Obstruction

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Distal ejaculatory duct obstruction (EDO) is a rare but potentially reversible cause of male infertility, accounting for approximately 1%–5% of cases among infertile men. The condition may present as complete, partial, or functional obstruction, with etiologies classified as either congenital—such as Müllerian duct cysts and atresia—or acquired, including ejaculatory duct cyst, post-infectious scarring, or ejaculatory duct calculi. Clinically, EDO is often suspected in men with azoospermia or severe oligoasthenospermia, low-volume ejaculate, acidic pH, and absent or diminished (partial obstruction) seminal fructose, in the presence of normal endocrine profiles and testicular volume. Symptomatic manifestations such as hematospermia and post-ejaculatory pelvic or perineal pain may also be present. Transrectal ultrasonography (TRUS), with or without seminal vesicle aspiration, remains the cornerstone of noninvasive diagnosis, replacing more invasive modalities like vasography. Imaging findings typically include dilated seminal vesicles, midline cysts, or calcifications. In selected cases, magnetic resonance imaging (MRI), or chromotubation may offer additional diagnostic clarity, particularly in complex or functional cases. The mainstay of definitive management is transurethral

resection of the ejaculatory ducts (TURED), first described in 1973, which aims to restore ductal patency and improve fertility outcomes. A systematic review comprising 29 studies and 634 patients demonstrated that TURED significantly improves semen volume in a median of 83% of patients, with concurrent gains in sperm concentration (62.5%) and motility (63%). Natural pregnancy was achieved in approximately 25% of cases, and up to 40% of patients could transition from in vitro fertilization (IVF) to intrauterine insemination (IUI) due to enhanced semen parameters postoperatively. The efficacy of TURED was particularly pronounced in patients with congenital and partial EDO, whereas outcomes were more limited in complete or acquired obstructions, likely due to irreversible secondary epididymal damage. Alternative or adjunctive approaches cyst (Müller) aspiration has shown promise in anatomically favorable or refractory cases. Despite the encouraging efficacy data, complication rates following TURED, including epididymitis, hematuria, or watery ejaculate, remain non-negligible (~10%), underscoring the need for patient selection and postoperative surveillance. In conclusion, EDO represents a surgically remediable form of obstructive azoospermia with measurable improvement in reproductive outcomes when accurately diagnosed and appropriately managed.

Keywords: Azoospermia, Ejaculatory Ducts, Infertility, TURED

I-5: The Association of The Seminal Microbiome on Male Infertility

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Recent research highlights the seminal microbiome's pivotal role in male fertility, with dysbiosis—an imbalance in microbial composition—linked to impaired spermatogenesis and infertility. Healthy semen typically harbors commensals, which support sperm function. However, dysbiosis characterized by elevated *Prevotella*, *Gardnerella*, *Escherichia coli*, and *Mycoplasma* species correlates with decreased sperm, motility, concentration, and morphology. Studies reveal that up to 40% of infertile men exhibit microbial shifts, with *Prevotella* abundance significantly higher in oligoasthenoteratozoospermic men. Pro-inflammatory responses triggered by pathogenic microbes may lead to oxidative stress. Moreover, elevated cytokine levels such as IL-6 and TNF- α in seminal plasma have been directly linked to microbial imbalance and may have a pathogenic role. These findings suggest that microbial profiling of semen may offer diagnostic and therapeutic potential in managing male infertility, emphasizing the need for further investigation into microbiome-targeted interventions to restore reproductive health. This talk will focus on the role of the seminal microbiome in male infertility.

I-6: Varicocelelectomy in Men with Non-Obstructive Azoospermia: A Controversial Therapeutic Strategy

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Background: Non-obstructive azoospermia (NOA) is a severe

form of male infertility characterized by impaired spermatogenesis. Varicocele, a common comorbidity in infertile men, has been proposed as a potentially correctable factor in NOA. However, the role of varicocele in this subset remains debated. Objective: To critically review the current evidence and expert opinions regarding varicocele in men with NOA, focusing on histological predictors, sperm recovery rates, and clinical outcomes.

Materials and Methods: A literature review was conducted using PubMed and Scopus databases, focusing on studies assessing testicular histopathology, sperm appearance in ejaculate post-surgery, and sperm retrieval rates in subsequent testicular sperm extraction (TESE). Clinical guidelines and expert consensus statements were also evaluated.

Results: Some studies report that varicocele may lead to the appearance of sperm in the ejaculate in up to 30–40% of NOA cases, particularly in men with hypospermatogenesis or late maturation arrest. Others show no significant benefit in patients with Sertoli-cell-only syndrome. Critics argue that surgery delays definitive assisted reproductive treatments and may provide false hope. Moreover, heterogeneity in study design, patient selection, and histological classification impedes conclusive interpretation.

Conclusion: Varicocele in NOA remains a controversial option. While potential benefits exist, especially in selected histopathological subtypes, the lack of robust randomized trials and standardized protocols limits universal recommendations. Shared decision-making and individualized assessment are essential until stronger evidence is available to resolve ongoing debates.

I-7: Single Gene Disorders in Male Infertility

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Male infertility is a complex condition with a significant genetic basis, affecting up to 15% of couples of reproductive age globally. Current clinical genetic testing for male infertility typically includes karyotyping, Y-chromosome microdeletion screening, and *CFTR* gene mutation analysis, particularly in cases of azoospermia and severe oligozoospermia. Single-gene disorders, resulting from pathogenic variants in individual genes, often exhibit clear patterns of Mendelian inheritance. However, the genetic architecture of spermatogenesis is highly complex- over 2,000 genes are believed to play critical roles in spermatogenesis and sperm maturation. Therefore, it is challenging to predict the number of single gene mutations that may lead to infertility and address all of them comprehensively. Mutations in these genes may cause spermatogenic aberrations directly or through gene–gene or genotype–environmental interactions. This complexity makes it challenging to identify all causative mutations and to fully understand the breadth of monogenic contributions to infertility. Next-generation sequencing (NGS) technology enables the rapid and simultaneous sequencing of billions of DNA bases, making it a valuable tool for detecting genetic variations linked to male infertility. This talk will emphasize the importance of single-gene disorders in male infertility, with particular attention to well-characterized genes such as *CFTR*,

AR, and *FSHR*. It will also explore genes involved in critical cellular processes -including cell division and development, DNA repair and recombination, and apoptosis- that are implicated in specific pathophysiological mechanisms contributing to impaired male fertility.

I-8: Unexplained Male Infertility Reasons

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Animal Biotechnology

I-9: Alternative Solution (Dry) for Gamete Storage in Farm and Endangered Animals

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Recently, an increasing number of studies have focused on the development of alternative, non-cryogenic methods for spermatozoa storage, with lyophilization (freeze-drying) emerging as the preferred approach. Dry storage offers several advantages over traditional deep freezing in liquid nitrogen, including lower costs, enhanced safety, and reduced environmental impact. However, large-scale studies involving livestock or other large animals -crucial for generating data applicable to human assisted reproduction- have been lacking. In my talk I will report for the first time the successful production of offspring from embryos fertilized using lyophilized spermatozoa

I-10: A Conserved Fertilization Complex Bridges Sperm and Egg in Vertebrates

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Background: Fertilization, the basis for sexual reproduction, culminates in the binding and fusion of sperm and egg. Although several proteins are known to be crucial for this process in vertebrates, the molecular mechanisms remain poorly understood.

Materials and Methods: We performed an AlphaFold-Multimer *in silico* screen against a library of 1,400 zebrafish-testis-expressed secreted/transmembrane proteins. We validated the predictions *in vivo* using immunoprecipitation-mass spectrometry experiments from zebrafish sperm lysates.

Results: We identified the protein Tmem81 as part of a conserved trimeric sperm complex with the essential fertilization factors Izumo1 and Spaca6. We demonstrate that Tmem81 is essential for male fertility in zebrafish and mice. In line with trimer formation, we show that Izumo1, Spaca6, and Tmem81 interact in zebrafish sperm and that the human orthologs interact *in vitro*. Notably, complex formation creates the binding site

for the egg fertilization factor Bouncer in zebrafish.

Conclusion: Together, our work presents a comprehensive model for fertilization across vertebrates, where a conserved sperm complex binds to divergent egg proteins -Bouncer in fish and JUNO in mammals- to mediate sperm-egg interaction.

Keywords: Fertilization, Sperm, Egg, AlphaFold, Fertility

I-11: Male Germline Complementation in NANOS2 Null Sheep and Cattle

McLean ZL^{1,2}, Fermin LM¹, Appleby SJ^{1,3}, Wei J¹, Meng F¹, MacLean PH¹, Perry BJ¹, Brophy B¹, Turner P¹, Forrester-Gauntlett B¹, Wells DN¹, Snell RG², Laible G¹, Oback B^{1,3*}

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Controlling the male germline drives genetic improvement in livestock breeding. To multiply the male germline, we aimed to produce germ cell-deficient 'host' males and rescue their germline by complementation with wild-type embryonic 'donor' cells. Cas9 genome editing was used to disrupt NANOS2, a key regulator of male germ cell development in male (NANOS2^{+/-}, NANOS2^{-/-}) and female (NANOS2^{-/-}) ovine fetal fibroblasts via gRNA-Cas9-mediated homology-directed repair. Targeted cell strains and wild-type controls were used to produce cloned offspring for breeding and phenotyping. Male homozygous knockout clones lacked detectable germ cells, while the somatic compartment of the testis remained intact. By contrast, male monoallelic and female biallelic targeting of NANOS2 did not affect germline development, resulting in fertile animals capable of producing fertile offspring with normal reproductive performance. The germ cell niche in NANOS2^{-/-} hosts was most efficiently complemented by aggregating compacted morulae, rather than earlier cleavage stages, resulting in 97% blastocyst chimaerization. Embryo-complemented cloned lambs from two different donor cell lines showed variable chimaerism across tissues from each germ layer, including various degrees of germline colonization. A subset of germline chimaeras contained normal numbers of prospermatogonia, indicating that the germline was fully restored for absolute transmission of the donor cell genotype. For disrupting NANOS2 in cattle, we introduced dual gRNA/Cas9 editors plus a repair template into IVF zygotes, producing three edited male and four edited female calves from biopsy-screened embryos. Two male calves and one female calf were homozygous for the precise 357bp knockout deletion. All other calves, including one heterozygous male, were mosaic, carrying additional alternatively edited alleles as determined by quantitative single cell genotyping. Confirming the sheep phenotypes, knockout bulls were sterile, and knockout cows were fertile. Our findings advance a novel breeding approach that integrates embryo-based complementation with genomic selection for exclusive dissemination of selected embryo genotypes.

I-12: Aptamers in Viral Therapy: "In Vitro Studies"

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Aptamers are molecules of single-stranded DNA or RNA that have a high affinity and specificity for binding to a variety of target molecules. They are frequently called "chemical antibodies" because they perform similar functions to monoclonal antibodies, but they have a number of benefits, such as stability, ease of synthesis, modification, and decreased immunogenicity. Viruses cause fatal diseases and seriously affect every host, from bacteria to humans. One of the presently available antiviral drugs is dominated by small molecules that specifically bind to the viruses, such as aptamers. In this experiment, we prepared aptamers against IHN (a fish virus) and SARS-CoV-2 (a human virus) using the SELEX method. Specific identified aptamers were used against IHN and SARS-CoV-2 viruses in EPC and Vero cell cultures. The results showed that aptamers successfully inhibited the proliferation of viruses in cell cultures. According to the results, aptamers were highly promising for antiviral therapy *in vitro* assay, and we will try to use these aptamers in animal viral infection models.

I-13: Polygenic Risk Score for Embryo Selection: Ethical and Legal Considerations

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Recent developments in reproductive genetics have enabled the use of polygenic risk scores (PRS) in embryo selection, expanding the scope of pre-implantation genetic testing (PGT) beyond monogenic and chromosomal conditions. While PGT has traditionally been used for detecting serious heritable disorders, the application of PRS introduces complex ethical, legal, and social considerations due to its probabilistic nature and potential use for non-medical traits. Ethical concerns include the risk of societal eugenics, stigmatization of disabilities, and challenges to equity and social justice. The clinical utility of PRS remains limited due to genetic determinism, pleiotropy, and population bias, particularly for individuals of non-European descent. Legally, regulatory frameworks vary widely, from permissive models (e.g., USA) to disease-based approaches (e.g., UK, Italy), and emerging proposals such as the welfarist model. International instruments, including the Oviedo Convention and EU regulations like the GDPR and AI Act, offer guidance but leave gaps regarding the commercial use of PRS and patient information rights. This presentation calls for a society-wide dialogue on responsible use, improved data governance, and adaptive regulation in response to rapidly evolving technologies in reproductive genetics.

I-14: Fertility and Infertility in Elite Athletes

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Background: With the rise in global participation in elite-level sports, concerns about infertility among high-performing athletes are gaining attention. While moderate physical activity supports reproductive health, excessive training may disrupt the hypothalamic–pituitary–gonadal axis, leading to hormonal imbalances, menstrual disturbances, and impaired spermatogenesis. These disruptions can reduce fertility and, in some cases, contribute to clinical infertility.

Objective: To examine the impact of elite-level athletic training on fertility and infertility in male and female athletes, with a focus on underlying mechanisms such as relative energy deficiency in sport (REDs), oxidative stress, and hormonal dysfunction.

Materials and Methods: A literature search was conducted using PubMed, Google Scholar, and Web of Science.

Results: In elite sportswomen, intense training frequently leads to menstrual dysfunction—including amenorrhea and luteal phase defects—primarily due to low energy availability affecting GnRH pulsatility. Although cycle restoration is possible with energy balance, age-related oocyte decline increases infertility risk. In male athletes, particularly those engaged in endurance sports, high training volumes are associated with reduced semen quality, elevated sperm DNA fragmentation, and increased oxidative stress. These changes may impair fertility and contribute to infertility, although some may be reversible with reduced training and recovery. Across sexes, moderate exercise supports fertility, while excessive intensity or insufficient recovery increases infertility risk.

Conclusion: Elite-level training exerts a dual impact—enhancing or impairing fertility depending on training load, recovery, and nutrition. Infertility in this population is often multifactorial, involving hormonal, metabolic, and oxidative pathways. Preventive strategies, including monitoring for REDs, optimizing nutrition, and early reproductive planning or fertility preservation, are crucial for mitigating infertility risks and preserving fertility in elite athletes.

Keywords: Reproductive Health, Fertility, Elite Athletes

I-15: Ethical and Legal Issues of Third Party Assisted Reproduction: Iranian Experience

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Third-party reproduction (TPR) means making babies for infertile couples using donated eggs, sperm, or embryos, or a surrogate. As someone other than couples must interfere in reproduction there are many ethical, legal and religious issues in this procedure. In Islamic countries, there are two main branches of Islam: Sunni and Shiite. Sunni Muslims ban all kinds of TPR because they believe it is similar to adultery and the lineage of the resulting baby is under question. Shiite Muslims don't believe in similarity of TPR to adultery so, do not consider it forbidden "HARAM" but Shiite Muslims also have ques-

tions about the lineage "NASAB" of the resulting children. In this context, for Sperm and embryo donation in which, sperm comes from a man other than the husband, donor is considered as father. On the mother side, as the mother shares in two part: oocyte and pregnancy, some clergy scholars believe that mother is the owner of the oocyte and others believe that the mother is who bears the child. No consensus is made in this regard. Among all the Islamic countries, TPR is practiced only in Iran and Lebanon. In Lebanon legal lineage is accepted. It means that genetical link between parents and children is not criterion for lineage. In Iran story is different. Although Iran has embryo donation law, but even in this law lineage is silent, so, the recipients are not considered as real parents. If the donors claim for the child, the court has no way except giving back the child to them as has happened in a court case in Mazandaran. Executive regulation of this law tried to solve this problem by insisting on anonymity. It means that none of the recipients must not know the donors' identity and donors don't know about the recipients. It no body knows where the child is, no claim can be made. But in IVF centers, anonymity is not completely followed and if some one searches for the recipients or donors' identity, can find them but with some difficulties. Considering the recipients always cannot be considered as real parents and legal lineage is not accepted in Islamic context, many problems may happen as follows: 1. claim for the resulting child, 2. blackmailing the recipients, 3. family name and ancestry, 4. religious problems, 5. nationality, 6. intimacy, 7. inheritance, 8. guardianship, 9. custody. Also, many ethical and legal problems happen about payment and also anonymity between resulting child and the donor(s). Many believe in the right to know the biological parents for any child but it may cause many legal problems. Surrogacy has less lineage related problems. It can be concluded that we need to accept the legal lineage to prevent any threat to recipient families and protect the children rights.

Keywords: Donation, Surrogacy, Religious, Lineage, Legal

I-16: Fertility Free Fall

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Global fertility rates have declined significantly over recent decades. According to the United Nations, the global fertility rate fell from 5.0 children per woman in 1950 to 2.3 in 2021, and it is projected to further decrease to 2.1 by 2050. Sub-replacement fertility (below 2.1 children per woman) is now prevalent in most high-income and many middle-income countries. For example, South Korea reported a record-low total fertility rate (TFR) of 0.72 in 2023, while the TFR in the European Union was 1.46 in 2022. Factors driving this trend include increased access to education and contraception, urbanization, rising female labor force participation, and socio-cultural changes. Voluntary childlessness is also becoming a relevant issue. The demographic consequences of declining fertility rates include aging populations, shrinking labor forces, and increased old-age dependency ratios, which may strain pension systems, healthcare infrastructure, and long-term economic growth. Countries may face reduced innovation and productivity as younger cohorts diminish in size. In response, some governments are implementing pronatalist policies, though their long-term outcomes remain uncertain.

Embryology

I-17: Influence of Uterine Immune Profiling and Tailored Therapeutics on Outcomes Following Single Blastocyst Transfer: A Matched Pair Study

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Introduction: Although assisted reproductive technologies (ART) have made substantial progress, approximately 70% of transferred embryos still fail to implant, leading to considerable emotional and economic consequences. Emerging data from randomized controlled trials and large cohort analyses emphasize the importance of the endometrial immune landscape in enhancing ART success. Uterine immune profiling assesses specific cytokine markers in the endometrium to identify immune dysregulation. When abnormalities are detected, personalized embryo transfer protocols are implemented to align treatment with the individual's immune profile. As prior research often combined different embryo stages and transfer types, the isolated impact of immune profiling on single day-5 blastocyst transfer remains insufficiently defined.

Materials and Methods: This matched-pair analysis focused on patients who underwent uterine immune profiling between January 1, 2020, and June 30, 2023, followed by a single day-5 embryo transfer (SET) with tailored treatment where necessary. These cases were matched 1:1 with controls who received SET without prior immune evaluation between 2018 and 2023. Matching criteria included maternal age (± 1 year), ART history (retrieval and transfer count), fertilization method (IVF/ICSI), transfer type (fresh/frozen), and blastocyst expansion grading (B1-B2, B3-B4, B5-B6). The primary outcome was live birth rate (LBR), with implantation and miscarriage rates as secondary endpoints.

Results: A total of 328 patients (164 per group) were analyzed, with 59 receiving fresh and 105 receiving frozen-thawed embryos in each cohort. The LBR was significantly higher in the immune-profiled group (41%) compared to controls (25%, $p < 0.001$). The benefit was most pronounced in frozen-thawed transfers [OR: 3.66 (1.9–6.8), $p = 0.001$], whereas no significant difference was observed in fresh transfers [OR: 0.92 (0.43–1.9), $p = 0.82$]. Non-top-quality blastocysts showed improved outcomes with the personalized approach [OR: 1.9 (1.02–3.5), $p = 0.04$], whereas top-quality embryos did not reach statistical significance [OR: 1.8 (0.87–4.1), $p = 0.1$]. In the frozen cohort, enhanced LBR was associated with both increased implantation [OR: 2.79 (1.6–4.8), $p = 0.0002$] and reduced miscarriage rates [OR: 0.39 (0.15–0.96), $p = 0.04$]. Both patients with and without a history of repeated implantation failure (RIF) benefited from individualized management [RIF: OR: 3.2 (1.2–8.4), $p = 0.01$; non-RIF: OR: 1.8 (1.07–3.2), $p = 0.02$].

Conclusion: This study supports the implementation of uterine immune profiling and personalized therapeutic strategies in the context of frozen embryo transfers, particularly when transferring non-top-quality blastocysts. The findings advocate for extending this approach beyond patients with RIF, highlighting its broader potential in optimizing ART outcomes.

I-18: Creating A Transformative Strategy for Infertility Treatments by Assessing Gamete and Embryo Metabolism Via Novel Non-Invasive Metabolic Imaging, Lab On-A-Chip & Artificial Intelligence Technologies

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Background: Selecting the most suitable gametes and embryos for implantation and subsequent healthy live birth is crucial to the success rate of assisted reproductive technologies (ARTs) and offspring health. Besides morphological evaluation using optical microscopy, a promising alternative is the non-invasive imaging of live gametes and embryos to establish metabolic activity performance. In recent years, metabolic imaging has been investigated using highly advanced microscopy technologies such as fluorescence-lifetime imaging microscopy (FLIM) and hyperspectral microscopy, however, yet cost and complexity limit its reach. In this project, we aimed to investigate the development and application of light-sheet on-a-chip microscopy, advanced microscopy and microsystem approaches as novel strategy for non-invasive metabolic imaging in ART.

Materials and Methods: Microsystems were fabricated following a standard UV-photolithography and two-photolithography, integrating light-sheet and bright-field/fluorescence microscopy into microsystems, including on-chip micro-lenses. Advanced research imaging systems such Light-sheet, FLIM and confocal microscopy were also used to assess early oocyte and embryo development, effect of aging and metabolic activity inhibition (FK866 inhibitor). Super-ovulated F1 (CBA/C57Bl6) mice were used to produce oocytes and two-cell embryos for embryo culture experiments. The safety of the approaches was investigated by assessing early development and viability of live oocytes and embryos after in-vitro culture, including a control, sham controls for culture conditions and live birth rate assessments. Study groups were assessed by non-invasive metabolic imaging to investigate autofluorescence of nicotinamide adenine dinucleotide NAD(P)H, flavin adenine dinucleotide (FAD) and the optical redox ratio (ORR) levels, using arbitrary units of autofluorescence (AU). Convolutional neural network model using metabolic images was also trained.

Results: Light-sheet on-a-chip devices could obtain high-resolution 3D images of their metabolic activity. The system allowed fast imaging of the embryos (< 2 s), while keeping a low dose of light exposure ($16 \text{ J} \cdot \text{cm}^{-2}$ and $8 \text{ J} \cdot \text{cm}^{-2}$). Optimum settings showed 30 times higher signal-noise-ratio images compared to confocal system ($P < 0.00001$; t-test). Results showed no significant differences between the control, illuminated and non-illuminated embryos for oocyte and embryo development, embryo quality and live birth rates ($P > 0.05$). Embryos with inhibited metabolic activity showed a 47% reduction in metabolic activity measured by metabolic imaging ($P < 0.0001$). The obtained metabolic images of two-cell embryos predicted blastocyst formation with an AUC of 0.974. A significant decrease in NAD(P)H levels was observed in the inner cells mass (ICM) of blastocyst from old females (Young: $424,6 \pm 26,0 \text{ AU}$; Old: $280,7 \pm 43,6 \text{ AU}$; $p < 0.05$). Furthermore, an increased metabolic activity in the ICM of blastocyst from old females was also observed (ORR Young: $901,5 \pm 6,2 \text{ AU}$; Old: $937,0 \pm 7,3 \text{ AU}$; $p < 0.05$). Light-sheet imaging revealed individual single cell

metabolic in blastocyst embryos. Furthermore, micro-optical systems allowed a 600nm resolution, including fluorescence imaging of mouse embryos at 2-cell, 4-cell, and 8-cell stages, resolving subnuclear chromatin and submicron tails and head of human spermatozoa.

Conclusion: The light-sheet on-a-chip and microsystems approaches are novel, thus, potential future applications could be developed for ART. The overall cost-efficient fabrication of the devices can facilitate scalability and integration into future devices. Metabolic imaging applications allow monitoring of early development with safe application using low doses of light.

Keywords: Light-Sheet on-A-Chip, Microsystems, Metabolic Imaging, Embryo Quality, Artificial Intelligence

I-19: Embryo Selection for Transfer (Past, Present, Future)

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A successful *in vitro* fertilization (IVF) cycle journey is being recognized with the delivery of a healthy baby following an embryo transfer and definitely choosing the right embryo plays a major role in this success. Currently, embryo selection is based on the morphological status of the embryos in most IVF labs plus the genetic test results along with the patient preference, which leads the treatment team to make the right decision to choose an embryo among others. With the assistance of Artificial Intelligence and other non-invasive methods like metabolomics, non-invasive genetic tests and spectroscopy, there is a promising future in front of the patient who are looking to have a successful IVF cycle. Utilizing these methods is not possible to all labs as some are expensive and some are in experimental phase yet.

I-20: Clinical and Operational Advantages of the Fertilite® Microfluidic Sperm Separation Chip (SSC)

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The Fertilite® Sperm Separation Chip (SSC), developed and manufactured in Iran, represents a modern advancement in sperm selection technologies for assisted reproductive treatments. This microfluidic device offers a centrifuge-free alternative to conventional methods such as Swim-Up (SU) and Density Gradient Centrifugation (DGC), enabling the isolation of highly motile, morphologically normal, and DNA-intact sperm. A multicenter post-market clinical follow-up (PMCF) study conducted across three major IVF centers in Iran, including Arash Women's Hospital, Erfan Niayesh, and Mehr Rasht, compared SSC to DGC and SU in 150 patients. Each sperm sample was split and processed via all three methods, with outcome metrics including post-processing motility, fertilization rate, cleavage rate, blastocyst formation, and implantation rate. Key findings highlight the SSC's superior performance: Post-processing sperm motility consistently reached 99%, outperforming DGC (75–85%) and SU (65–70%). Fertilization rates with SSC exceeded 95% across most cases. Cleavage and blastocyst formation rates were elevated, often above 90% and

70% respectively. Clinically, SSC has proven especially effective in challenging cases, including male factor infertility, high DNA fragmentation index (DFI), recurrent pregnancy loss (RPL), and testicular sperm aspiration (TESA/PESA) samples. Operationally, the chip offers additional advantages: no centrifugation (reducing oxidative stress), standardized processing time (~20–30 minutes), ease of use, and cost efficiency. These features make SSC highly suitable for diverse IVF lab environments, particularly in resource-limited or high-throughput settings. The Fertilite® SSC thus emerges as a validated, scalable solution that enhances reproductive outcomes while simplifying sperm preparation workflows. It holds promise for broader adoption in both local and international fertility clinics.

Keywords: Microfluidic Sperm Separation, Assisted Reproductive Technology, Fertilite® Sperm Separation Chip, Male Infertility Treatment, IVF Outcomes

I-21: MicroRNAs in The Blastocoel Fluid as Accessible Indicators of Chromosomal Normality

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Background: MicroRNAs (miRNAs) derived from the pre-implantation blastocoel fluid (BF) have attracted interest as accessible biomarkers indicative of embryonic health in ongoing IVF cycles. Therefore, we investigated expression levels of some aneuploidy-associated miRNAs and implantation-related miRNAs as predictive markers for embryo chromosomal normality. **Materials and Methods:** In this study, the BF of 25 blastocysts that had been checked for aneuploidy (aneuploid=17 and euploid=8) was aspirated and the expression of 10 miRNAs (miR-20a, miR-30c, miR-661, miR-372, miR-142, miR-191, miR-345, miR-339, miR-141, and miR-27b) and four genes (ERBB4, SELL, ITGB3, ITGAV) were evaluated using real time-PCR.

Results: Results showed that the levels of miR-661 and miR-20a were significantly higher in the BF of the aneuploid embryos compared to the euploid group ($P=0.0017$ and 0.004 , respectively). A comparison of the mRNA levels between the aneuploid and euploid groups also demonstrated a significant difference in ITGAV ($P=0.013$) and SELL ($P=0.0317$) levels. In the euploid group, a negative correlation was found between ITGB3 and miR-30c ($r = -0.71$, $P=0.08$), and in the aneuploid group, a positive correlation was found between ERBB4 and miR-345 ($r = 0.71$, $P=0.02$).

Conclusion: It can be suggested that miR-20a, miR-661, and ITGAV levels of BF could be used as less-invasive biomarkers to evaluate embryonic health. Moreover, aneuploidy-related miRNA levels were associated with levels of genes involved in embryo implantation.

Keywords: Blastocoel Fluid, miRNAs, In Vitro Fertilization, Implantation, Biomarker

I-22: Embryo Selection beyond Morphology: Opportunities and Challenges of Time-Lapse Monitoring

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Today in the field of *In Vitro* Fertilization (IVF), there are new technologies and innovations which aim to the increase of efficiency of IVF treatments and therefore, to the amelioration of the percentage of pregnancy. Due to the continuous amelioration of the culture systems, we can support the in vitro development of the embryo from the zygote to the blastocyst stage. During a traditional IVF cycle, a highly experienced Clinical Embryologist records the morphological features by observing the embryos outside of the culture incubators, which causes:

- Disturbance of culture conditions (temperature, pH, CO₂, osmolarity)
- Stress of the embryos
- Focused evaluation of the embryo morphology and the stage of embryo development
- Dispersed observations on the embryos, loss of numerous information concerning their development, acting negatively on the embryo survival and the further outcome of pregnancy.

The Time Lapse technology is an innovation used for the in vitro embryo culture and the choice of the most suitable embryo for embryotransfer. It offers a continuous viewing on the embryo development inside a specific incubator equipped with a digital micro-camera and a high quality software, taking photos of it every 5-10 minutes and creating an individualized video. By this way, we can achieve an uninterrupted culture and isolate different facts (the timing of each mitotic division and different morphokinetic parameters of the embryo). The use of an algorithm contributes to the exclusion of some embryos and to the selection of the best embryo for embryotransfer. In combination with the Artificial Intelligence algorithms, it offers a much greater possibility to select the most suitable embryo, contributing to the single embryo transfer policy.

I-23: Preparedness and Continuity of Care in IVF Laboratory during Natural and Infrastructural Disasters

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Catastrophic events can severely threaten the integrity of gametes, embryos, cryo-storage systems and data recording mechanisms. IVF centers must be prepared to confront natural and man-made disasters. This can be done through emergency plans and rapid response protocols that are practiced using regular drills. Any emergency plan should contain safety and protection protocols for patients and personnel, for fresh and cryo-preserved patient's tissue and IVF materials as well as patient's data records, laboratory records, financial and operational documents. Key elements to any emergency plan include risk identification and assessment, proactive infrastructure reinforcement, validated backup systems (power, gas, cryopreservation), and integrated environmental monitoring. Should preventative measures such as staff cross training fail, a comprehensive emergency plan must include response and continuity sections which detail necessary steps during and after disaster. Incident documentation, appropriate communication protocols with patients and authorities as well as post disaster validation are among the core components. In this presentation, we will dive deeper into existing quality management frameworks and their integration of contingency plans with a focus on proactive risk assessment, redundancy planning, and rapid response protocols.

I-24: Challenges in Assisted Reproductive Technology

(ART): An Introduction

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This abstract provides a concise overview of the key challenges currently facing the field of Assisted Reproductive Technology (ART). While ART has revolutionized infertility treatment and facilitated parenthood for millions, its continued evolution is met with significant hurdles across clinical, ethical, and psychosocial domains. Clinically, challenges include optimizing ovarian stimulation protocols, uterine immune profile, embryo euploidy, mitigating the risks of multiple pregnancies, and improving success rates for specific patient populations, such as those with advanced maternal age or recurrent implantation failure. Application of add-ons for improving the ART success rate is always a challenging and hot issue. The financial burden associated with ART, which often lacks comprehensive insurance coverage, represents a major accessibility challenge for many prospective parents. There is also technological limitations such as limited gamete and embryo selection accuracy, success in vitro maturation of oocyte, cryopreservation risks, laboratory errors, equipment failure, and dependence on advanced infrastructure. Furthermore, a complex landscape of ethical dilemmas persists, encompassing issues such as the disposition of unused embryos, the implications of third-party reproduction (egg, sperm, and embryo donation), and the increasing use of preimplantation genetic testing. Finally, the psychosocial impact on patients -including emotional distress, relationship strain, and the pressure to succeed- demands greater integration of mental health support into fertility care. It is promising that new technologies are in progress to solve some of these challenges and improve the success rate of ART techniques. Addressing these multifaceted challenges is crucial for enhancing the safety, accessibility, and efficacy of ART, ultimately ensuring that it continues to serve individuals and couples seeking to build their families.

I-25: Psychologic Aspect Challenges in ART Specially Couples Suffering from RIF

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1. Emotional Stress and Anxiety

Infertility stress: ART is usually pursued after a period of unsuccessful conception, often accompanied by long-term emotional distress.

Uncertainty: The unpredictability of outcomes (success/failure of treatment cycles) creates ongoing anxiety.

Cycle rollercoaster: Hormonal medications and treatment cycles cause emotional ups and downs.

2. Depression and Grief

Failed cycles: Repeated failed attempts can lead to deep disappointment, hopelessness, or clinical depression.

Loss of pregnancy or embryos: Grief over miscarriages, still-

births, or decisions to discard embryos can be intense.

Loss of “natural” parenthood: Some may mourn the inability to conceive or give birth naturally.

3. Relationship Strain

Couple conflict: Differing coping styles or treatment expectations can strain relationships.

Sexual intimacy: Scheduled intercourse and performance pressure can affect sexual relationships.

Family dynamics: External pressure or unsolicited advice from family members may create tension.

4. Identity and Self-worth Issues

Gender identity challenges: For many, fertility is deeply tied to masculinity or femininity, and ART can evoke feelings of inadequacy.

Guilt and shame: Especially if one partner is the identified cause of infertility.

5. Ethical and Moral Concerns

Embryo decisions: Choices about surplus embryos, genetic testing, or selective reduction may conflict with personal or religious values.

Third-party reproduction: Using donors or surrogates can raise identity, attachment, and moral concerns.

6. Financial Pressure

ART treatments are often expensive and may not be covered by insurance. The financial burden can cause:

- Stress and anxiety
- Conflict between partners
- Feelings of guilt over money spent without guaranteed results

7. Stigma and Social Isolation

Cultural pressure: In some societies, childlessness is stigmatized, especially for women.

Secrecy: Couples may keep ART treatment private, leading to isolation and lack of social support.

Judgment: Fear of judgment over non-traditional routes to parenthood (e.g., surrogacy, donor eggs/sperm).

8. Psychological Challenges in Donors and Surrogates

Attachment issues: Surrogates may face emotional difficulty letting go of the child.

Identity concerns: Donors might wonder about future contact or the well-being of genetic offspring.

Motivation concerns: If financial reasons dominate, ethical and psychological concerns may arise later.

9. Post-birth Issues

Parental attachment: Some parents fear difficulty bonding, especially in cases of donor conception.

Disclosure dilemmas: Whether and how to tell the child about donor conception or surrogacy can cause anxiety.

Identity questions (for children): Donor-conceived children may later face their own psychological struggles with identity and origins.

10. Need for Psychological Support

Professional counseling is often recommended to:

- Prepare individuals emotionally before treatment
- Provide support during treatment
- Help cope with outcomes (success or failure)
- Guide third-party reproduction processes ethically and compassionately

I-26: Sperm DNA Fragmentation and How to Reduce It

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Semen quality plays a crucial role in the success of assisted reproductive technologies (ART). The prognosis of ART outcomes is influenced by multiple factors, with sperm DNA fragmentation (SDF) emerging as a key parameter affecting fertilization, embryo development, and pregnancy rates. This presentation provides an overview of semen analysis and highlights the clinical significance of SDF in patients with poor ART prognosis. It discusses the negative impact of high DNA fragmentation on sperm function and reproductive outcomes, emphasizing the importance of selecting appropriate laboratory methods to reduce DNA damage. The objective is to explore devices, techniques, and strategies that can help decrease SDF. The presentation focuses on sperm quality, preparation methods, and advanced sperm selection tools, including individual sperm selection approaches. The session concludes with practical take-home messages on how to reduce sperm DNA fragmentation using lab technologies, antioxidant supplements, and optimized protocols to improve ART results.

Female Infertility

I-27: The Role of The Female Factor in Unexplained Infertility

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Unexplained infertility (UI) is a diagnosis of exclusion, defined by the inability to achieve pregnancy after 12 months of regular, unprotected intercourse, despite a standard infertility workup revealing normal ovulation, semen analysis, tubal patency, and uterine cavity. While UI affects approximately 15-30% of infertile couples, the underlying pathophysiology remains poorly understood. UI is not a single entity, but rather a spectrum of subtle defects in female reproductive physiology that evade conventional diagnostic tests. Key areas of focus include: 1) Ovarian Dysfunction: investigating subtle defects in folliculogenesis, oocyte quality, and chromosomal integrity that are not detected by standard hormonal assays or ultrasound. Evidence suggests a potential role for mitochondrial dysfunction, oxidative stress, and impaired meiotic machinery. 2) Endometrial Receptivity: examining abnormalities in the endometrial microenvironment, including aberrant gene expression of implantation markers (e.g., HOXA10, LIF), immunologic dysregulation (e.g., natural killer cells), and altered endometrial microbiome composition that compromise embryo-endometrial crosstalk. 3) Embryo-Maternal Crosstalk: exploring the complex signaling pathways between the developing embryo and the endometrium, highlighting how subtle disruptions in this communication can lead to implantation failure. The potential impact of lifestyle factors, such as advanced maternal age and environmental exposures, on these underlying mechanisms will be discussed. Understanding of these female factors, particularly at the molecular and cellular level, is crucial for moving beyond the UI diagnosis and developing more targeted, personalized therapeutic strategies to improve reproductive outcomes for affected couples.

I-28: The Role of FIGO Type 3 Fibromas on IVF Outcomes

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Uterine fibroids, or leiomyomas, are benign smooth muscle tumors that frequently affect women of reproductive age. The International Federation of Gynecology and Obstetrics (FIGO) classification system categorizes fibroids based on their location, with type 3 myomas defined as intramural fibroids that contact the endometrium but do not distort the uterine cavity. The impact of FIGO type 3 fibroids on *in vitro* fertilization (IVF) outcomes remains a subject of ongoing debate due to their proximity to the endometrium despite a seemingly normal cavity. Recent studies suggest that type 3 fibroids may adversely affect implantation and pregnancy rates by disrupting endometrial receptivity, altering local vascularization, and inducing an inflammatory environment. Some observational data indicate lower clinical pregnancy and live birth rates in women with untreated type 3 myomas undergoing IVF compared to controls without fibroids. However, evidence remains limited and heterogeneous, with few randomized controlled trials available. Surgical removal via hysteroscopic or laparoscopic myomectomy may improve IVF outcomes in select patients, particularly those with a history of implantation failure or thin endometrium. Current guidelines recommend individualized decision-making, taking into account fibroid size, symptoms, and reproductive history. Further high-quality studies are needed to clarify the precise role of FIGO type 3 fibroids in infertility and to define the optimal management strategy prior to IVF. In conclusion, while type 3 fibroids do not directly distort the uterine cavity, their close relationship to the endometrium suggests a potential negative impact on IVF outcomes that may justify surgical intervention in selected cases.

I-29: Restoring Fertility in Women with POI and DOR: From Conventional IVA to Next-Generation, Less Invasive Techniques

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Ovarian dysfunction is a condition characterized by a decrease in residual follicles in the ovaries, classified into POI (premature ovarian insufficiency) and DOR (Diminished ovarian reserve). POI is characterized by amenorrhea before the age of 40, whereas DOR shows hormonal abnormalities but does not necessarily involve menstrual irregularities or ovulation disorders. Previously, POI was considered to affect 1% of women, but recent studies indicate an increased prevalence of 3.7%. Infertility treatment for ovarian dysfunction using patients' own genetic eggs is challenging. The only established method is embryo transfer to POI patients using eggs obtained from young healthy donors fertilized with the partner's sperm. However, this method is not ideal due to ethical issues and potential immunological abnormalities from carrying a non-genetically related pregnancy. It is also prohibited in some countries and regions for religious or other reasons. In POI, activation of dormant primordial follicles arrests, and recruitment of developing follicles does not occur, resulting in the absence of FSH-responsive antral follicles, leading to anovulation and infertility.

In DOR, the number of developing follicles decreases due to reduced ovarian reserve, resulting in fewer FSH-responsive antral follicles and minimal oocyte retrieval even with aggressive controlled ovarian stimulation. The speaker has developed *in vitro* activation (IVA) treatment to induce activation of dormant primordial follicles and growth of early follicles in the FSH-independent phase, enabling POI/DOR patients to conceive with their own genetic eggs. IVA involves laparoscopic removal of ovaries or ovarian tissues, followed by *in vitro* ovarian tissue culture for follicle activation, and subsequent grafting into and around the residual ovary. The initial method required two laparoscopic surgeries due to 48-hour *in vitro* ovarian tissue culture. To reduce the invasiveness, a method that can be completed in a single surgery has been implemented, known as drug-free IVA. Further research is ongoing to develop less invasive methods, some of which will be introduced in this lecture.

I-30: Derivation of Bovine Embryonic Stem Cells and Exploring Their Differentiation Potential *In Vivo*

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Bovine pluripotent stem cells (PSCs) hold significant potential for diverse applications in agriculture, reproductive biotechnology, and biomedical research. However, challenges persist in establishing stable bovine PSC lines and understanding the mechanisms underlying their pluripotency maintenance. Here, we derived bovine embryonic stem cells (bESCs) from Holstein cattle embryos. These cells exhibited robust differentiation capacity into three germ layers *in vitro* and *in vivo*. Transcriptome analysis revealed distinct molecular profiles compared to primed-state bESCs. Notably, bESC proliferation ceased on methanol-treated feeder cells, in contrast to mouse ESCs (mESCs), which proliferated normally. Pathway analysis identified key signaling events critical for bESC survival and proliferation, highlighting species-specific regulatory mechanisms. Furthermore, the derived bESCs demonstrated chimerism capacity in early bovine embryos, underscoring their functional pluripotency. This work provides a foundation for advancing bovine embryology research and stem cell-based biotechnologies in livestock.

Genetics

I-31: Genomic Architecture of Human Reproductive Behaviour

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Unlike rare Mendelian disorders, common complex traits or diseases, also known as multifactorial or polygenic disorders, are controlled by complex network of environmental and genetic factors. It is only in recent years that unraveling the black

box of genomic architecture of complex traits has been feasible leading to successful discovery of thousands of SNP-trait associations. Human reproductive behavior is a new topic of research across the medical, social and biological sciences. Since reproductive behaviour is shaped by biology and environment, a multidisciplinary approach is required to understand the common genetic aetiology and how it relates to health, reproductive biology, environment and externalising behaviour. The timing of onset of human reproductive behaviour can be measured by Age at First Birth (AFB) and Age at First Sexual intercourse (AFS). The success of human reproductive behaviour can be measured by Number of children Ever Born (NEB) and childlessness. AFB, AFS, NEB and childlessness are all complex traits and are partially controlled by genetic factors. Childless individuals and those with a low NEB are a heterogeneous group consisting of involuntary and voluntarily childless. Although therapeutic options for infertility in the form of Assisted Reproductive Technology (ART) are available, they are highly ineffective at later ages. A better understanding of the genetic architecture of human reproductive behavior and its relation to the environment would enable the discovery of predictors of infertility, which would in turn greatly improve family planning but also reduce costly and invasive ART treatments. Here we show how bioinformatics tools and systems biology approaches can support analysis of high-throughput biological data, promising gains in knowledge of multifaceted biological mechanisms underlying human reproductive behavior. Besides, recent advances in the field promise successful stratification of people based on their genetic background and potential risks of childlessness, even years before their reproductive ages. This approach, so-called personalized medicine, promises appropriate translation of bioinformatics research into medical practice.

I-32: Transforming Reproductive Medicine: The Power of Liquid Biopsy, Genomics and Artificial Intelligence

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Current embryo genetic testing techniques have evolved beyond traditional targeted testing to encompass genome-wide analysis through massively parallel sequencing. Haplarithmis, enables simultaneous haplotyping and copy-number profiling from single cells, improving diagnostic accuracy and resolution of preimplantation genetic testing (PGT). This method supports clinical applications such as direct point mutation detection, parental-origin assessment of aneuploidies (PGT-AO), and mitochondrial heteroplasmy detection (PGT-MT). Recent advancements allow for comprehensive PGT based solely on parental samples or a single embryo biopsy, with base-pair resolution and increased efficiency, minimizing false negatives and maximizing embryo classification precision. The future of PGT lies in automation, integration, and non-invasive diagnostics. Predictive models powered by multimodal deep learning are emerging to enhance embryo selection by combining genomic and morphological data. Similarly, all-in-one non-invasive (NIPT) approaches can lift the current NIPT screening programs and avoid invasive follow ups. During my talk, I will describe how convergence of these innovations is set to

revolutionize reproductive medicine. A paradigm that improves success rates, reduces unnecessary interventions, and fosters personalized, predictive, and preventive reproductive care.

I-33: From Single Loci to Whole Genomes: The Evolution of Preimplantation Genetic Testing

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High-throughput single-cell genotyping technologies have revolutionized preimplantation genetic testing (PGT). By enabling the simultaneous interrogation of hundreds of thousands of informative single nucleotide polymorphisms (SNPs) across the entire embryonic genome, these advancements have shifted clinical practice from traditional targeted single-locus methods to genome-wide genotyping and haplotyping of embryo biopsies. Initially driven by SNP-array platforms, this comprehensive approach—often termed universal or all-in-one PGT—allows for the simultaneous detection of monogenic disorders, aneuploidy, and structural chromosomal aberrations from a single biopsy using a standardized protocol. More recently, the integration of whole genome sequencing (WGS)-based analyses further expanded diagnostic capabilities and is gradually being adopted in clinical settings. The aim of this presentation is to give an overview on the evolution of PGT technologies, from SNP arrays to WGS. In addition to analytical advantages and pitfalls, the presentation will also briefly address a number of potential ethical concerns surrounding genome-wide PGT technologies.

I-34: The role of PGS in IVF: Weighing its Benefits Against the Challenges of Overuse in Recurrent Implantation Failure and Recurrent Pregnancy Loss

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I-35: Empowering Infertility Treatments: Expanded Carrier Screening in Reproductive Medicine

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Expanded Carrier Screening (ECS) is a pivotal tool in reproductive genetics, particularly for infertile couples utilizing assisted reproductive technologies (ART). ECS identifies carriers of autosomal recessive and X-linked disorders, enabling informed reproductive decisions and reducing the risk of genetic conditions in offspring. Here, current guidelines and considerations for ECS in infertile couples will be reviewed, emphasizing on its integration with ART, counseling needs, and challenges. For infertile couples, ECS is crucial as it aligns with ART protocols, such as *in vitro* fertilization (IVF) combined with preimplantation genetic testing for monogenic disorders (PGT-M),

allowing selection of unaffected embryos. Guidelines from the American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics and Genomics (ACMG) recommend offering ECS to all individuals considering pregnancy, advocating a universal, tiered approach. The ACMG's Tier 3 screening, covering 97 autosomal recessive and 16 X-linked conditions, is recommended for all, ensuring equitable access across diverse populations. Key considerations for infertile couples include early ECS timing to inform ART cycles, comprehensive genetic counseling to address complex results (e.g., variants of uncertain significance), and exploration of reproductive options like PGT-M, donor gametes, or adoption. Conditions such as cystic fibrosis, linked to male infertility due to congenital bilateral absence of the vas deferens, are particularly relevant, with studies recognizing risks in infertile couples. ECS challenges include the financial burden (\$150 – \$400+), the complexity of result interpretation, and the emotional toll on couples navigating infertility. Despite these, ECS empowers couples by reducing genetic risks and enhancing ART outcomes. The shift to universal screening reflects increasing population diversity, moving away from ethnicity-based approaches. In conclusion, ECS is crucial for infertile couples, integrating genetic risk assessment with ART to improve reproductive health. Its effective implementation requires robust genetic counseling, emotional support, and equitable access to address the unique needs of the population. Ongoing research is needed to optimize ECS panels and counseling strategies.

Keywords: carrier screening, reproductive genetics, infertility

Imaging

I-36: Radiology Intervention in Ob & Gyn Disorders

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Oral Presentation

Andrology

O-1: The Effect of Sperm Preparation Techniques on the Biological Parameters, DNA Fragmentation, and Specialized Fertility Indices in Patients with Oligo-Astheno-Teratozoospermia

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Background: The prevalence of infertility in Iran is 18.3-22.5% (~20.3%) with a confidence interval of 95%, which is higher than the average global infertility rate (15%). Today, the importance of andrological indications in causing infertility has received more attention than gynaecological indications. The study aimed to evaluate the effect of four sperm preparation techniques, including Discontinuous Percoll Density Gradient Centrifugation (DGC), Albumin Gradient Filtration-1 (AGF-1), Albumin Gradient Filtration-2 (AGF-2), and swim-up methods, on the biological parameters, chromatin integrity, DNA fragmentation, and specific sperm fertility indices (SSFI) in patients with Oligo-Astheno-Teratozoospermia (OAT) and normozoospermia.

Materials and Methods: One hundred men with normozoospermia and OAT participated in the study. Before and after processing methods, biological parameters (concentration, velocity, total motility, and normal morphology), SSFI (PMSCa, PMSCb, MSC, SMI, and FSC), chromatin integrity, and DNA fragmentation were investigated using SQA-V Gold sperm analyzer, specific staining, TUNEL, and COMET assays.

Results: In OAT patients, the highest number of sperm exhibiting the best velocity, motility, PMSCa, PMSCb, and SMI were observed using the DGC method. Conversely, in normozoospermic patients, both the AGF-2 and swim-up processing techniques successfully separate spermatozoa with the highest biological parameters and SSFI. Sperm DNA damage was significantly reduced following preparation by DGC, AGF-2, and swim-up techniques. In patients with normozoospermia and OAT, the lowest levels of DNA damage and nuclear fragmentation were identified using the AGF-2 and DGC methods, respectively.

Conclusion: Choosing an effective technique for sperm preparation and recovering a highly functional sperm population in OAT and normozoospermia patients depends on the quality of the semen samples, the types and degrees of male infertility, the experience of the laboratory staff, the laboratory equipment, and the specific sperm parameters that require improvement for male infertility treatment.

Keywords: Sperm Preparation Technique, Biological Parameter, Sperm Fertility Indices, Oligo-Astheno-Teratozoospermia, Normozoospermia

Embryology

O-2: Effect of PRP on Antioxidative Status of Rat Ovarian Tissue after Induced Ischemia-Reperfusion

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Background: Ovarian torsion establishes a severe condition where blood flow is initially blocked and then abruptly restored, resulting in a spike of reactive oxygen species (ROS) and inflammatory mediators that may irreversibly harm ovarian follicles. This work investigated the efficacy of a single intraperitoneal injection of pure platelet-rich plasma (P-PRP), abundant in growth factors and cytokine modulators, in mitigating detrimental biochemical cascades in a rat model.

Materials and Methods: Thirty adult female Wistar rats were randomly assigned to five groups (n=6 per group): sham control, ischemia only (I), ischemia-reperfusion (I/R), ischemia plus PRP (I + PRP), and I/R plus PRP (I/R + PRP). P-PRP was generated using a standardized two-step centrifugation technique and administered (0.5 mL) 30 minutes prior to the surgical induction of ischemia or reperfusion. The right ovaries were removed for examination after three hours of ischemia, or after three hours of ischemia followed by three hours of reperfusion. Lipid peroxidation was evaluated using malondialdehyde (MDA) concentrations, while DNA oxidation was quantified using an 8-hydroxy-2'-deoxyguanosine (8-OHdG) ELISA. The total antioxidant capacity (TAC) and the activities of superoxide dismutase (SOD) and glutathione peroxidase (GPx) were measured spectrophotometrically, while the quantities of TNF- α and IL-6 were assessed using immunoassay.

Results: As anticipated, ischemia and I/R significantly increased MDA and 8-OHdG ($P<0.05$) while decreasing TAC, SOD, and GPx activities ($P<0.05$ vs. control), alongside notable elevations in TNF- α and IL-6. Both the I + PRP and I/R + PRP groups had a significant reversal of these effects: MDA and 8-OHdG levels decreased toward baseline, antioxidant enzyme activities increased, and pro-inflammatory cytokines were markedly diminished ($P<0.05$ vs. untreated I and I/R).

Conclusion: The data indicate that P-PRP provides significant antioxidant and anti-inflammatory protection in ovarian torsion, highlighting its potential as a minimally invasive therapeutic approach to maintain ovarian function following ischemia injury.

Keywords: Ovarian Torsion, Oxidative Stress, Platelet-Rich Plasma, Inflammatory Cytokines, Antioxidant Defense Mechanisms

O-3: The Safety and Efficacy of Stem Cell-Derived Gametogenesis in Human Infertility Treatment: A Systematic Review of Preclinical and Clinical Evidence

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Background: Stem cell-derived gametogenesis (SCDG) represents a paradigm shift in treating absolute infertility, yet its clinical translation remains controversial. This systematic review evaluates current evidence on SCDG's efficacy in generating functional gametes and its safety profile in human infertility treatment.

Materials and Methods: Following PRISMA guidelines, we searched PubMed, Embase, Web of Science, and clinical trial registries through 2021-2025. Included studies reported on SCDG (*in vitro* gametogenesis from pluripotent or somatic stem cells) in human or human-cell models. Outcomes included gamete functionality (maturation, fertilization competence), euploidy rates, and safety endpoints (epigenetic abnormalities, teratoma risk). Risk of bias was assessed using SYRCLE for preclinical and ROBINS-I for clinical studies.

Results: From 1,583 screened records, 68 studies (54 preclinical, 14 clinical) met inclusion criteria: Efficacy: Only 23% of studies achieved complete gametogenesis (oocytes: 18%; sperm: 28%). Human oocyte-like cells showed 12% maturation to MII (vs. 45% in controls); sperm-like cells demonstrated 31% fertilization competence in animal models. Safety: Pre-clinical studies reported epigenetic abnormalities in 41% of SCDG-derived gametes (vs. 9% controls). No human teratomas were reported, but 3 studies noted aberrant imprinting. Clinical Trials: Two Phase I trials (n=42) reported SCDG-derived embryo implantation rates of 11% (95% CI 5-21%), with no live births.

Conclusion: While SCDG demonstrates proof-of-concept, significant gaps persist in gamete functionality and safety. Current evidence does not support clinical application outside controlled trials. Prior to translation, standardization of differentiation protocols and long-term epigenetic studies are urgently needed. This review highlights both the revolutionary potential and key biological hurdles of SCDG.

Keywords: Stem Cells, In Vitro Gametogenesis, Infertility

O-4: Improving Mitochondrial Membrane Potential in Frozen Mouse Oocytes through Green Synthesis of Fe₃O₄/Honey Nanocomposites

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Background: Mitochondria, the first line of defense of vitrified oocytes, are severely damaged during cryopreservation. Infertility researchers are investigating ways to improve mitochondrial membrane potential. In this study, synthesized green honey (FHNC)-based Fe₃O₄ nanocomposites were used to improve mitochondrial membrane potential performance in immature mouse oocytes during cryopreservation.

Materials and Methods: Adult female NMRI mice were used to collect immature germinal vesicle (GV) oocytes. GVs were divided into three groups: non-frozen (nVit), frozen (Vit), and frozen with nanocomposite (Vit+NC). Immature oocytes were washed for 15 min in equilibration medium and then in freezing medium containing Fe₃O₄/Honey nanocomposite for 1 min. Finally, oocytes were transferred to liquid nitrogen using Cryotop. Seven days later, frozen oocytes were placed in warming medium containing different concentrations of sucrose. After two hours, they were transferred to oocyte maturation medium and incubated for 16-18 hours. The mitochondrial membrane potential of all three groups was examined by JC1 staining.

Results: Based on the obtained results, the level of reactive oxygen species in the Vit+NC group (3.76 mean ± 0.48 SEM) was significantly reduced compared to the vitrification group (7.67 mean ± 0.40 SEM). Furthermore, the level of reactive oxygen species was significantly increased in the Vit group (7.67 mean ± 0.40 SEM) compared with the nVit group (6.67 mean ± 0.48 SEM).

Conclusion: Fe₃O₄/Honey nanocomposites can improve mitochondrial membrane potential in frozen/warmed immature mouse oocytes.

Keywords: Vitrification, Nanocomposite, Honey, Mitochondrial Membrane Potential, Fe₃O₄

O-5: The Promising Role of Mesenchymal Stem Cells Seeded on Decellularized Scaffolds for Bioengineered Artificial Ovaries

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Background: Mesenchymal stem cells (MSCs) loaded onto decellularized scaffolds have recently drawn attention due to their potential to interact with the scaffold and regulate cell behavior in artificial ovaries. MSCs are a group of cells from mammalian and human bone marrow and blood, adipose tissue, umbilical cord, placenta, amniotic fluid, endometrium, and menstrual blood that could be isolated and cultured *in vitro*. According to studies, MSCs can promote ovary reconstruction through inhibition of granulosa cell apoptosis and follicular atresia. Pluripotent stem cells possess differentiation potential and the capacity for diversity of mesodermal phenotypes and tissue induction. Although MSCs cannot directly differentiate into oocytes, their transplantation enables to regulation of the nutrition and immunity of the artificial ovary by secreting cytokines and growth factors. This can induce stem cells such as embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs), and oogonial stem cells (OSCs) within the artificial ovary to differentiate into primordial germ cells (PGCs), germ cell-like cells, and oocytes. Also, Germline stem cells are able to promote steroid hormone production and support folliculogenesis.

Materials and Methods: Recent studies have revealed that transplanting the bioengineered ovary which made by loading

MSCs, ESCs, iPSCs, and OSCs onto the scaffolds can significantly increase sex hormone levels, follicle numbers, and granulosa cell proliferation, oocytes growth, follicle maturation, reproductive functionality, and fertility recovery after natural mating.

Results: Despite these pleasing outcomes, the application of iPSCs may enhance mitochondrial mutation risks, and more attention should be paid to pathogenic mitochondrial DNA alteration after transplantation.

Conclusion: In conclusion, recent research showcased that MSCs from various sources have become the most efficient cell type in clinical applications of cell therapies. The bright prospect of a breakthrough in the field of regenerative medicine provides the possibility of participation of MSCs in artificial ovary reconstruction to restore human fertility and ovarian endocrine function.

Keywords: Mesenchymal Stem Cells, Artificial Ovary, Tissue Engineering

O-6: Exosome-Mediated Sulforaphane Delivery Attenuates Testicular Damage in An Experimental Azoospermia Model

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Background: Azoospermia is a major cause of male infertility, often associated with oxidative damage and testicular structural abnormalities. Exosomes, a subset of extracellular vesicles with sizes ranging from 30 to 150 nm, offer a promising platform for targeted therapeutic interventions due to their biocompatibility and ability to cross biological barriers. This study aimed to evaluate the histopathological outcomes of intratesticular administration of sulforaphane-loaded exosomes in a rat model of azoospermia.

Materials and Methods: Exosomes were isolated from human serum and loaded with sulforaphane, a known antioxidant phytochemical, via ultrasonication. Azoospermia was induced in male rats using busulfan, and the rats were then divided into five groups: healthy control, azoospermia control, sulforaphane-only, exosome-only, and sulforaphane-loaded exosome groups. After eight weeks, testicular tissues were collected and histologically analyzed using hematoxylin and eosin staining, as well as Masson's trichrome staining.

Results: Dynamic light scattering and ultraviolet-visible spectrophotometry indicated successful entrapment of 47% of the sulforaphane within the exosomes. Histological evaluation of the sulforaphane-loaded exosome group revealed significant improvement ($P < 0.05$) in germinal cell layer counts -including spermatogonial stem cells, spermatocytes, and elongated spermatids- as well as recovery of spermatogenesis and enhanced epithelial integrity compared to the azoospermia and other treatment groups. Masson's trichrome staining showed notable amelioration of interstitial fibrosis and collagen deposition in the sulforaphane-loaded exosome-treated rats compared to the

other groups. These findings suggest that sulforaphane-loaded exosomes not only protect testicular tissue but also promote structural regeneration in azoospermia.

Conclusion: Our data highlight the potential of exosome-based sulforaphane delivery as a regenerative strategy for restoring testicular tissue structure in azoospermia. Further studies are warranted to investigate the underlying molecular pathways and long-term reproductive outcomes.

Keywords: Exosomes, Sulforaphane, Azoospermia, Testicular Histopathology, Male Infertility Therapy

O-7: MenSCs and Exosomes: A Novel Therapy for Mitochondrial Repair in Polycystic Ovary Syndrome

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Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder marked by hormonal and metabolic disruptions. Mitochondrial dysfunction, characterized by reduced ATP production, decreased mitochondrial DNA (mtDNA) copy numbers, and increased oxidative stress, impairs steroidogenesis and ovarian function. The PGC-1 α /NRFs/TFAM pathway, crucial for mitochondrial biogenesis, is often disrupted in PCOS. Menstrual blood-derived mesenchymal stem cells (MenSCs) and their exosomes, due to their non-invasive collection and regenerative properties, hold promise for restoring mitochondrial function through bioactive factors.

Materials and Methods: MenSCs were isolated from menstrual blood, cultured in DMEM/F12 with 10% FBS, and characterized by flow cytometry for positive markers (CD44, CD73, CD90, CD105) and negative markers (CD34, CD45). Exosomes were purified via ultracentrifugation and confirmed by Western blotting (CD63, CD9). PCOS was induced in female Wistar rats (6–8 weeks, 160 $\pm$ 20 g) using letrozole (1 mg/kg/day for 21 days). Rats were divided into four groups (n=8 each): • Control Group: Healthy rats received 1% carboxymethyl cellulose (vehicle) orally. • PCOS Group: PCOS-induced rats received intraovarian PBS injections to mimic surgical stress. • MenSCs Group: PCOS-induced rats received intraovarian injections of 1×10^6 MenSCs per ovary in 20 μ L PBS. • MenSCs-EXO Group: PCOS-induced rats received intraovarian injections of 60 μ g exosomes per ovary in 20 μ L PBS. After two weeks, ovarian tissues were analyzed for PGC-1 α (quantitative real-time polymerase chain reaction (qRT-PCR, immunofluorescence), NRF1/TFAM (Western blot), and mtDNA copy number (qPCR).

Results: MenSCs showed high expression of CD44, CD73, CD90, CD105, and low expression of CD34, CD45. In the PCOS group, PGC-1 α mRNA and protein levels were significantly reduced compared to controls, but both MenSCs and MenSCs-EXO treatments restored these levels, with exosomes showing a stronger effect. NRF1 and TFAM protein levels were lower in PCOS but increased significantly after MenSCs and MenSCs-EXO treatments, with exosomes demonstrating greater efficacy. mtDNA copy number was reduced in PCOS but showed improvement with MenSCs and a significant increase with MenSCs-EXO treatment.

Conclusion: MenSCs and their exosomes, validated by flow cytometry, effectively enhance mitochondrial biogenesis in PCOS by upregulating the PGC-1 α /NRFs/TFAM pathway and

increasing mtDNA copy numbers. MenSCs-EXO exhibited superior efficacy, offering a promising, targeted therapy for PCOS-related mitochondrial dysfunction, with significant potential for advancing reproductive medicine.

Keywords: Polycystic ovary syndrome (PCOS), Menstrual Blood-Derived Stem Cells (MenSCs), Exosomes, Mitochondrial Biogenesis

O-8: Lycopene Mitigates the Adverse Effects of Cryopreservation on Acrosome Reaction, Mitochondrial Membrane Potential and Sperm DNA Fragmentation in Asthenozoospermic Men during Freezing-Thawing

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Background: Human semen cryopreservation considered as indispensable part of assisted reproductive centers, andrology laboratories and sperm bank. This technique is associated with significant damage to sperm. Adding an antioxidant to the cryopreservation medium could effectively mitigate these adverse effects. Lycopene, a naturally occurring red carotenoid with potent antioxidant properties, has been shown beneficial effects on various sperm parameters. This investigation studied the effect of lycopene supplementation on Acrosome Reaction, mitochondrial membrane potential (MMP) and DNA fragmentation during the cryopreservation of semen samples from asthenozoospermic men.

Materials and Methods: Semen samples were collected from 30 asthenozoospermic men. Each sample was then divided into three groups: Control (fresh), Freeze (treated with cryoprotectant alone), and Freeze + Lycopene (treated with cryoprotectant and 5 µmol/L lycopene). The samples in the freezing groups were cryopreserved using a human sperm freezing medium and a rapid freezing method. For each sample, acrosome reaction with fluorescein isothiocyanate-labelled pisum sativum agglutinin (FITC-PSA) staining, MMP was evaluated using Rhodamine 123 staining, and DNA fragmentation was examined using SDA kit. Data were statistically analyzed using the repeated measures analysis method.

Results: Our results showed a significant increase in the mean level of sperm DNA fragmentation and also a significant decrease in the mean percentage of sperm with intact acrosome and sperm mitochondrial membrane potential in the freeze group compared to the control group ($P<0.001$). While in the freeze + lycopene group, a significant decrease in the mean level of sperm DNA fragmentation ($P<0.001$) and a significant increase in the mean percentage of sperm with intact acrosome ($P=0.003$) and mean sperm mitochondrial membrane potential ($P<0.001$) were observed compared to the freeze group ($P<0.001$).

Conclusion: Based on our results we concluded that lycopene reduces the adverse effects of cryopreservation on sperm quality in asthenozoospermic men.

Keywords: Asthenozoospermia, Cryopreservation, Lycopene

O-9: Effect of Pentoxifylline on Testicular Tissue Structure

and Spermatogenesis in Adult Mice Undergoing Chemotherapy with Etoposide

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Background: Etoposide, a DNA-damaging chemotherapeutic agent, effectively induces apoptosis in tumor cells but also has harmful effects on male fertility, including reduced testicular weight, impaired spermatogenesis, decreased sperm motility, and suppressed testosterone production. This study aimed to assess the antioxidant role of pentoxifylline in alleviating etoposide-induced damage to testicular tissue, spermatogenesis, and sperm quality in adult NMRI mice.

Materials and Methods: 24 adult male NMRI mice (average weight 35 ± 2 g) were randomly assigned to four groups ($n=6$): Control, Etoposide (1 mg/kg/day, i.p.), Pentoxifylline (100 mg/kg/day, i.p.), and a combined Pentoxifylline + Etoposide group, treated for 35 days. Body weight was recorded before and after treatment. After anesthesia and necropsy, sperm parameters, DNA damage (acridine-orange staining), and nuclear maturation (aniline-blue staining) were assessed using sperm from the left cauda epididymis. The left testis was processed for histological evaluation using hematoxylin & eosin staining and stereology, while the right testis was used to calculate daily sperm production (DSP). Serum testosterone, total antioxidant capacity (FRAP), and malondialdehyde (MDA) levels were also measured. Data were analyzed using one-way ANOVA and Tukey's post hoc test, with significance set at $P<0.05$.

Results: Etoposide treatment significantly reduced body and testis weight, sperm count, motility, viability, daily production, and tail length, as well as testicular tissue volume, seminiferous tubule dimensions, spermatogenesis indices, germ cell numbers, testosterone levels, and total antioxidant capacity ($P<0.05$). It also significantly increased serum MDA levels ($P<0.05$). However, no significant changes were observed in sperm DNA damage or nuclear maturation. Co-treatment with pentoxifylline significantly improved these parameters compared to the etoposide group.

Conclusion: The results of this study showed that pentoxifylline with its antioxidant properties could prevent the destructive effects of etoposide on testis tissue, spermatogenesis indices and sperm parameters by reducing oxidative stress, increasing total antioxidant capacity and serum testosterone level.

Keywords: Pentoxifylline, Etoposide, Testis, Spermatogenesis, Oxidative Stress

O-10: Sperm Selection by Chemotaxis toward Follicular Fluid Derived Extracellular Vesicles

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Background: Selection of most competent sperm for intracytoplasmic sperm injection (ICSI) is crucial for improving fertilization rate following assisted reproductive technique procedure. Up till now wide variety of methods have been used to select high quality spermatozoa for ICSI. By considering sperm chemotactic ability, high-quality spermatozoa with improved fertilization potential can be selected. This study focuses on selecting spermatozoa based on chemotaxis induced by extracellular vesicles (EVs) of follicular fluid (FF).

Materials and Methods: FFs of 10 women collected undergoing ovum pick-up procedure. The EVs were extracted by commercialized exosome isolation kit. EVs were encapsulated in agar palates in different concentration of EVs (5, 25 and 50 µg/ml) and sperm chemotaxis toward the chemoattractant agar plates were evaluated after 30 min of incubation. Sperm parameters including concentration, motility, progressive motility, and viability, and DNA integrity were evaluated following chemotaxis based sperm selection.

Results: The findings demonstrated that, incorporation of 50 µg/ml FF-MV in chemoattractant plates showed significantly higher sperm concentration, progressive motility and DNA integrity compared to control group ($P < 0.05$).

Conclusion: Our findings suggest that FF-EVs particularly at a concentration of 50 µg/ml possess significant chemoattractant properties that can selectively enrich sperm populations with improved parameters. These results highlight the potential of FF-EVs as a novel tool for selecting high-quality spermatozoa for ICSI procedure

Keywords: Sperm Selection, Chemotaxis, Extracellular Vesicles, Follicular Fluids

O-11: Protective Role of *Daucus Carota* and *Piper Nigrum* Against MTX-Induced Testicular Injury in Rats

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Background: Methotrexate (MTX), a common chemotherapy drug, causes testicular damage via oxidative stress, impairing male fertility. This study evaluated the protective effects of *Daucus carota* and *Piper nigrum* alcoholic extracts against MTX-induced testicular injury in rats, focusing on oxidative stress markers and tissue integrity.

Materials and Methods: In this experimental study, a total of 49 rats were randomly divided into seven groups, receiving MTX alone and in conjunction with different doses of *Daucus carota* extract (200 and 400 mg/kg), *Piper nigrum* extract (15 and 7.5 mg/kg), a combination of *Piper nigrum* (7.5 mg/kg) and *Daucus carota* (200 mg/kg), and a control group. The extracts were given orally through gavage starting one day before MTX treatment and continuing for two weeks. The study measured testosterone levels in the blood, Johnson's index, and the diameter of seminiferous tubules from tissue sections. It also assessed

markers of oxidative stress (ROS, Nitrite, MDA, GSH, CAT, SOD), as well as levels of MPO and mitochondrial membrane potential (MMP) and the consistency of testicular tissue.

Results: The result showed significant testicular tissue damage in the MTX-exposed group, as indicated by increased ROS, MDA, and Nitrite levels compared to the control group. Moreover, there were notable reductions in CAT, GSH, SOD, testosterone levels, Johnson's index, and seminiferous tubule diameter in the MTX-treated rats. However, treatment with extracts, especially *Piper nigrum* extract, significantly improved testicular damage and reduced oxidative stress markers compared to the MTX group.

Conclusion: In conclusion, the study suggests that alcoholic extracts of *Daucus carota* and *Piper nigrum* may help alleviate the harmful effects of methotrexate on testicular tissue, potentially offering a therapeutic option for male infertility due to chemotherapy-related testicular damage.

Keywords: *Daucus Carota*, *Piper Nigrum*, Methotrexate, Oxidative Stress, Testis

Female

O-12: Deep Learning-Based Analysis of Immunological Predictors in Recurrent Implantation Failure

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Background: The inability to conceive due to recurrent implantation failure (RIF) persists despite advancements in assisted reproductive technologies. In order to help identify RIF patients with immunological problems who might benefit from appropriate immunotherapy, the goal of this work was to build a deep learning model to stratify these patients and predict the implantation outcome.

Materials and Methods: We included 2,463 RIF patients who did not have any gynecological or anatomical abnormalities that were referred to a clinical immunologist and received appropriate immunotherapies. In order to construct a deep learning (TabNet) model to predict live births, 23 factors including age, body mass index, vitamin D3, TSH, Th1/Th2 ratio, CD3, CD16, CD19, CD56, CD3/CD4, CD3/CD8, CD16/56, antiphospholipid, anticardiolipin, anti-β2 glycoprotein, anti-tissue transglutaminase (anti-TTG), ANA, anti-ds-DNA, anti-TPO, anti-TG, smoking, alcohol, and embryo quality were leveraged. The characteristics of the groups that experienced implantation failure and live birth were compared using statistical analysis. A confusion matrix, a receiver operating characteristic (ROC) curve, and calibration plots are used to assess the model's performance.

Results: Our model predicted the implantation's outcome with the accuracy of 87% and the area under the curve (AUC) was 0.9417. The model indicated that the Th1/Th2 ratio, CD3/CD8, anti-TTG, CD3, and CD19 were the most significant character-

istics when all variables were present.

Conclusion: Using the combinations of 23 variables, such as autoantibodies, thyroid antibodies, lymphocyte subsets, embryo quality, and other markers, the TabNet model produced satisfactory results in predicting live births in RIF patients. This can help identifying the subset of RIF patients, with no anatomical and gynecological anomalies, who may benefit from immunomodulation therapies.

Keywords: Recurrent Implantation Failure, RIF, Deep Learning, Risk Factors, Prediction Model

Genetics

O-13: Decoding Hidden Risks in Biological Parents: Intelligent Leveraging of Comparative Whole Exome Sequencing

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Background: Since the revolution sparked by with the first *in vitro* fertilization (IVF) birth, reproductive medicine has experienced remarkable evolution. Numerous technologies have been developed to enhance IVF success rates, reduce treatment failures, and mitigate pregnancy-related risks. Recent efforts have focused on improving the selection of high-quality gametes and embryos prior to uterine transfer. Emerging exosome-based methods, non-invasive flux measurements via bioelectrical micro-sensors, and co-culture engineering strategies demonstrate considerable promise. However, when conventional treatments fail, gamete or embryo donation remains a last resort.

Materials and Methods: Donor selection is typically limited to families with at least two healthy children and no history of severe genetic disorders. Yet, self-reported donor health data may be incomplete or inaccurate, especially when financial incentives motivate donors.

Results: The occurrence of offspring born with severe, untreatable conditions -such as major brain developmental anomalies accompanied by cranial dysmorphology- despite no reported teratogenic exposures or related events during pregnancy, raises serious concerns. These outcomes inflict profound emotional distress on families and impose substantial burdens on health-care systems.

Conclusion: Advanced genetic approaches, including comparative whole exome sequencing of biological parents, offer the potential to identify carriers of deleterious alleles and prevent their transmission to offspring. When combined with comprehensive prenatal screening, this strategy may enhance the safety and efficacy of infertility treatment. Nonetheless, continuous evaluation and long-term follow-up of assisted reproductive technology outcomes remain essential.

Keywords: Comparative Whole Exome Sequencing, Biological Parents, Gamete Donation, Embryo Donation

O-14: EGCG Loaded Nanostructured Lipid Carriers (NLC) Enhances Receptivity Potential of Endometrial Cells via LIF and HOXA10 Upregulation

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Background: Implantation failure is one of the main obstacles in assisted reproductive technology (ART) cycles. Identifying a novel strategy to enhance uterine receptivity could improve the implantation rate. The present study aims to develop nano-structured lipid carriers (NLCs) as a delivery system to improve the bioavailability of epigallocatechin gallate (EGCG), thereby enhancing its effect on endometrial receptivity.

Materials and Methods: EGCG-loaded NLCs were prepared using the hot homogenization technique. The mean particle size, polydispersity index (PDI), and zeta potential (ZP) were determined using dynamic light scattering (DLS). Morphological behaviors were observed with scanning electron microscopy (SEM). The endometrial Ishikawa cell line was treated with the produced nanoparticles, and the expression of several endometrial receptivity markers was evaluated by real-time polymerase chain reaction (RT-PCR).

Results: The nanoparticles with particle size of 85 nm, zeta potential of 21 mV, and encapsulation of 83% were prepared. Analysis of RT-PCR results showed the enhancing mRNA of Leukemia inhibitory factor (LIF) and HOXA10 in EGCG-treated endometrial cells. Results also confirmed the higher influence of EGCG-loaded NLC-RGD on gene expression patterns in comparison to EGCG. However, the expression of Integrin beta-3 (ITGB3) and insulin-like growth factor-binding protein 1 (IGFBP1) was not affected.

Conclusion: The results showed that EGCG bioavailability increased by loading into NLC. Using NLC as a carrier to deliver EGCG to endometrial cells is an effective approach to improve endometrial receptivity. Upregulation of LIF and HOXA10 is the probable mechanism by which EGCG enhances the endometrial receptivity potential.

Keywords: EGCG, Endometrium Receptivity, LIF, HOXA10

O-15: Identification of Chromosome Segregation-Related Mutations through Trio Whole Genome Sequencing in Consanguineous Couples with Recurrent Pregnancy Loss and Aneuploid Fetuses

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Background: Recurrent pregnancy loss (RPL) affects 1–2% of couples and is linked to chromosomal abnormalities, uterine factors, and thrombophilia. Consanguinity increases the risk of autosomal recessive disorders, elevating the likelihood of pregnancy loss. Although fetal aneuploidy is prevalent, the contribution of novel recessive variants in conjunction with aneuploidy remains underexplored. This study applies whole genome sequencing (WGS) to identify candidate genes involved in embryonic development and chromosomal segregation, offering insights into RPL in consanguineous families.

Materials and Methods: Two consanguineous couples with RPL were analyzed using trio-based WGS on parental blood and aneuploid products of conception (POC), confirmed by array CGH. Variants with low read quality, benign classification, or allele frequency >1% were excluded. Women over 37 were omitted to reduce age-related aneuploidy. Pathogenicity was assessed using ACMG guidelines. Functional analysis focused on genes related to embryonic development, chromosome segregation, and placental function, using gene ontology and model organism data. Key variants were validated by polymerase chain reaction and Sanger sequencing.

Results: WGS identified novel candidate genes including *WDR20*, *SNX9*, *SVEP1*, *CROT*, *CHMP4A*, and *SLC25A14*, and novel variants in *NRP1*, *COL4A3*, *RAD21*, *KIF9*, *VCAM1*, *ZG16*, and *DES*, potentially contributing to RPL in consanguineous couples. Several genes harbored homozygous recessive mutations in affected fetuses. Disruptions in *WDR20*, *SNX9*, *ZG16*, *RAD21*, and *KIF9* may impair chromosome segregation and lead to aneuploidy. Mutations in *COL4A3* and *SVEP1* may affect placental development. *CROT*, *CHMP4A*, and *SLC25A14* influence mitochondrial metabolism, while *NRP1*, *VCAM1*, and *DES* affect vascular and extracellular matrix integrity, further impairing placental function. Two likely pathogenic variants in *CROT* and *DES* were identified, along with eleven variants of uncertain significance. Animal studies support the roles of these genes in implantation, placentation, and embryonic survival.

Conclusion: Through trio WGS, we identified 6 novel genes and 7 novel variants mainly linked to embryonic development and chromosomal segregation, highlighting contributors to RPL.

Keywords: Recurrent Pregnancy Loss (RPL), Whole Genome Sequencing (WGS), Novel Candidate Genes, Consanguinity, Aneuploidy

Poster Presentation

Andrology

P-1: Improvement of Human Sperm Quality in Elderly Men by Aqueous Extract of *Chlorophytum borivilianum*: An In Vitro Study

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Background: Male fertility tends to decline with age, often accompanied by reduced sperm motility, viability, and increased DNA fragmentation. *Chlorophytum borivilianum* (commonly known as Safed Musli) is a traditional medicinal plant with antioxidant and fertility-enhancing properties. This study aimed to assess the *in vitro* effects of *C. borivilianum* extract on sperm quality in aged men.

Materials and Methods: An aqueous extract of *Chlorophytum borivilianum* roots was prepared by macerating the powdered roots in distilled water, followed by gentle heating, filtration, and freeze-drying to obtain a dry extract. Semen samples were collected from 30 healthy men over the age of 50. Each sample was divided into four aliquots: a control group and three treatment groups incubated with the extract at concentrations of 50, 100, and 200 µg/ml for 1 hour at 37°C. Sperm motility, viability, and morphology were assessed based on WHO 2010 guidelines. DNA fragmentation was evaluated using the TUNEL assay.

Results: The extract demonstrated a dose-dependent improvement in total and progressive motility. A significant enhancement in sperm viability and a reduction in DNA fragmentation were observed in the treatment groups compared to the control, particularly at the 200 µg/ml concentration ($P < 0.05$).

Conclusion: *Chlorophytum borivilianum* extract may positively influence sperm quality in aged men *in vitro* and holds potential as a natural agent for supporting male fertility in advanced age.

Keywords: Sperm Quality, *Chlorophytum Borivilianum*, Male fertility, Aged men

P-2: Redox Imbalance and Its Role in Sperm DNA Integrity: A Systematic Review of Oxidative Stress-Induced Fragmentation

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Background: The primary factor behind male infertility is oxidative stress (OS), as it leads to sperm DNA fragmentation (SDF). The presence of reactive oxygen species (ROS) damages the sperm chromatin structure, resulting in apoptosis, reduced fertility potential, and adverse effects on assisted reproductive technology (ART) outcomes. Research indicates that oxidative stress is directly correlated with DNA fragmentation in sperm cells, affecting both idiopathic and secondary male infertility cases.

Materials and Methods: The research study implemented PRISMA guidelines as its methodology. The research team conducted database searches of PubMed, ScienceDirect, and Scopus for studies between January 2020 and March 2025. The research used “oxidative stress,” “sperm DNA fragmentation,” and “male infertility” as its search terms. The study included original research and systematic reviews that analyzed human sperm, oxidative biomarkers, and SDF assays (TUNEL, SCSA, Comet). Twelve studies were selected after quality appraisal using the AMSTAR 2 and Newcastle-Ottawa tools.

Results: The research established a steady positive relationship between seminal ROS concentrations and SDF rates in men with fertility issues. The study by demonstrated that a DNA fragmentation index (DFI) above 30% correlated with increased 8-OHdG and lipid peroxidation markers in semen plasma. The research by demonstrated that SDF strongly influenced pregnancy loss rates, especially when oxidative imbalance persisted. The therapeutic use of antioxidants resulted in substantial DFI reductions from 32.5% to 15.0% when patients consumed CoQ10, selenium, and vitamin E supplements for two months.

Conclusion: The relationship between SDF and oxidative stress biomarkers in male infertility is well established. The clinical application of oxidative assays and DNA fragmentation testing will improve diagnosis and help guide antioxidant therapy. Future research should focus on establishing standardized thresholds for DFI and ROS across different populations.

Keywords: Oxidative stress, Sperm DNA fragmentation, Reactive oxygen species, Male infertility, DNA fragmentation index

P-3: The Relationship Between HSPA2 Gene Expression in Sperm And Intrauterine Insemination Outcome

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Background: Intrauterine insemination (IUI) is one of the infertility treatments with a success rate of around 10%. Heat shock protein A2 (HSPA2) is a protein present on the head of sperm and plays a role in the production and maturation of sperm. HSPA2 rearranges two other important proteins (SPAM1-ARSA) and this Triplex complex plays a key role in sperm oocyte interaction. This study was conducted to investigate the relationship between sperm *HSPA2* gene expression and IUI outcome.

Materials and Methods: Thirty thousand couples whose wives are candidates for IUI are enrolled in this ongoing cohort study and followed up till 2 weeks later for serum beta HCG test. Couples' body mass index (BMI) was less than 30 kg/

m2. The ages of couples were <49 & <40 years old for Men & women, respectively. Men with varicocele, leuKocytospermia, or reproductive system infections were not enrolled. On the day of the IUI cycle, the non-processed part of the semen sample is received from the embryology lab of Royan Institute. After washing sperms with phosphate-buffered saline (PBS), RNA extraction from sperms was done using the TRIzol method, and cDNA was synthesized using the SMObio kit. HSPA2 gene expression was quantitatively compared with the housekeeping gene (β -actin) using the SYBR green and $2^{-\Delta\Delta CT}$ method. According to the IUI outcome, gene expression was compared between the IUI success & IUI failure groups.

Results: Till now, 9 couples in the IUI success group and 30 couples in the IUI failure group were enrolled. The mean $\pm$ SD of HSPA2 gene expression was 1.604 ± 1.02 and 1.152 ± 1.00 in the IUI success and IUI failure groups, respectively. Although gene expression was increased in the IUI success group, but this difference was not statistically significant ($P=0.076$).

Conclusion: According to preliminary data, this sample size is not enough for a conclusion. Sampling of this study will be continued until reaching 30 couples in each group.

Keywords: Intrauterine insemination, HSPA2, Fertilization, Gene expression, Real-time PCR

P-4: Impact of Zeta Potential Technique on Sperm DNA Fragmentation Index Based on SCSA

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Background: The DNA fragmentation index (DFI), representing the proportion of sperm with damaged DNA, has been identified as a crucial factor influencing overall clinical outcomes. The zeta potential technique is an advanced method used in assisted reproductive technologies (ART) to select high-quality sperm based on their surface electrical charge. The sperm chromatin structure assay (SCSA) evaluates DNA damage by measuring sperm susceptibility to acid-induced denaturation, acridine orange staining, and flow cytometry. In addition to DFI, SCSA also measures high DNA stainability (HDS). This study aims to assess the effect of zeta potential-based sperm selection on reducing sperm DNA fragmentation.

Materials and Methods: The pre-post study was conducted on 30 infertile men with a high DNA fragmentation index ($DFI > 25\%$) and at least one previous failed IVF cycle. Semen samples were processed using the zeta potential technique, and sperm DNA fragmentation and HDS were assessed using the SCSA. Statistical analysis was performed using the paired samples t-test. Significance was determined using a p-value threshold of 0.05.

Results: The results of the SCSA showed that the mean percentage of sperm with no fragmentation before sperm preparation using the zeta potential method was $53.37 \pm 0.15\%$, and after preparation, it increased to $56.27 \pm 0.14\%$ ($P=0.010$). The average percentage of total DFI before and after zeta potential

selection was $46.63 \pm 0.15\%$ and $43.47 \pm 0.14\%$, respectively, with a significant difference ($P=0.009$). There was no statistically significant change in the mean percentage of HDS before and after sperm preparation ($P=0.919$).

Conclusion: The study showed that zeta potential sperm selection significantly increases the concentration of sperm with higher DNA integrity and reduces the total DFI, which may in turn contribute to improved ICSI outcomes.

Keywords: Infertility, DNA fragmentation, Sperm selection, SCSA

P-5: Effects of RHO Kinase Inhibitor on Sperm Parameters During Four Hours of Incubation at 37 °C

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Background: Infertility affects approximately 15 % of couples globally, with male factors contributing to over half of cases. Sperm preparation techniques, including centrifugation and incubation, cause an increase in oxidative stress and induce apoptosis. Therefore, in this study, we aimed to evaluate the effects of RHO kinase inhibitor (Y-27632) as an apoptosis inhibitor on sperm parameters during incubation at 37 °C for 4 hours.

Materials and Methods: Semen samples from 20 normozoospermic men were divided into four groups: a control group and three treatment groups with 5, 10, and 20 μ M Y-27632. After incubation for 4 hours in a 37 °C CO₂ incubator, sperm parameters including motility, viability, membrane integrity, and DNA fragmentation were assessed.

Results: The 5 μ M Y-27632 group showed a significant increase in total motility (from 45.40% to 75.60%), progressive motility (from 24.66% to 84.10%), and membrane integrity (from 78.13% to 86.50%) ($P<0.05$). DNA fragmentation increased significantly in the 20 μ M group (18.80%) compared to the control (11.70%) ($P<0.05$). No significant differences in viability were observed among the study groups.

Conclusion: Low-dose of Y-27632 (5 μ M) improved sperm motility and membrane integrity without increasing DNA damage, suggesting potential clinical use of RHO kinase inhibitor in sperm processing procedure. However, higher concentrations of RHO kinase inhibitor could exert detrimental effects on sperm parameters.

Keywords: RHO Kinase Inhibitor, Y-27632, Sperm Processing, Sperm Parameters

P-6: Melatonin Enhances The Quality of Asthenozoospermic Sperm during The Freezing–Thawing Process by Mitigating Oxidative Stress, DNA Fragmentation, and Spontaneous Acrosome Reactions

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Background: Sperm cryopreservation, crucial for assisted reproductive technologies (ART), often leads to cellular damage due to reactive oxygen species (ROS) during the freeze-thaw process. Asthenozoospermia, defined by sperm motility below 40%, is a common cause of male infertility. Sperm from asthenozoospermic men are more vulnerable to cryo-damage due to higher ROS levels. This damage, including oxidative stress, DNA fragmentation, and acrosomal dysfunction, affects sperm quality and fertilization. This study aimed to assess melatonin's protective effects in reducing ROS, DNA fragmentation, and spontaneous acrosome reactions.

Materials and Methods: Semen samples were collected from thirty asthenozoospermic men between November 2023 and May 2024 at the Amir al-Momenin Infertility Center, Arak, Iran. Samples were divided into three groups: fresh (control), freeze, and freeze + melatonin (1 mM). A rapid freezing protocol with human sperm freezing medium was used. Intracellular ROS was measured using a ROS kit (KiaZist, Iran) by flow cytometry. DNA fragmentation was assessed using the Halo-sperm kit (Ideh Varzan Farda, Iran), and acrosome reaction was evaluated using FITC-PSA staining (Sigma, USA). Data were analyzed using the Repeated Measures Analysis method.

Results: Compared to the control group, the freeze group showed significantly increased mean ROS levels, DNA fragmentation, and acrosome reaction ($P=0.010$). Melatonin-treated samples exhibited a significant reduction in mean ROS ($P=0.005$), percentage DNA fragmentation ($P=0.015$), and acrosome reaction ($P=0.004$) compared to the freeze group.

Conclusion: The results indicate that the addition of melatonin during sperm cryopreservation significantly reduces oxidative stress, preserves DNA integrity, and stabilizes the acrosome in asthenozoospermic sperm. These findings highlight the potential role of melatonin as a protective agent to improve the efficiency of ART.

Keywords: Melatonin, Asthenozoospermia, Freeze-Thaw, DNA Fragmentation, Oxidative Stress

P-7: Papaverine Mitigates Cryopreservation-Induced Oxidative Stress and Membrane Damage in Asthenozoospermic Men without Altering Spontaneous Acrosome Reaction

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Background: Asthenozoospermia, defined by reduced sperm motility (<42%, WHO 2021), is a primary cause of male infertility. Sperm cryopreservation, essential for assisted reproductive technologies (ART), induces cryoinjury through excessive reactive oxygen species (ROS) production during freeze-thaw cycles. This results in oxidative stress, membrane damage, and impaired sperm function, particularly in asthenozoospermic men. This study evaluated the effects of papaverine on sperm acrosome reaction, membrane integrity, and intracellular ROS levels in cryopreserved samples from asthenozoospermic men.

Materials and Methods: Semen samples were collected from 30 asthenozoospermic men at the Amir-AL-Momenin Infertility Centre in Arak, Iran, in 2023. The samples were divided into three groups: control (fresh), freeze, and freeze + papaverine (100 μ M). Cryopreservation in the freeze groups was performed using a rapid freezing protocol. Membrane integrity was evaluated using the hypo-osmotic swelling (HOS) test, acrosome reaction was assessed by fluorescein isothiocyanate-labeled *Pisum sativum* agglutinin (FITC-PSA) staining, and intracellular reactive oxygen species (ROS) levels were measured using the DCFH-DA dye and flow cytometry. Data were analyzed statistically using the repeated measures analysis method.

Results: Cryopreservation significantly decreased membrane integrity ($P<0.001$) and increased acrosome reaction ($P<0.004$) and ROS levels ($P<0.001$) compared to fresh samples. Treatment with papaverine significantly improved membrane integrity ($P<0.001$) and reduced ROS levels ($P<0.040$) compared to the freeze group. However, papaverine had no significant effect on reducing the rate of acrosome reaction ($P>0.127$).

Conclusion: Our results indicate that adding papaverine to the cryopreservation medium can protect asthenozoospermic sperm by reducing oxidative stress, minimizing spontaneous acrosome reactions, and improving membrane integrity. These effects highlight papaverine's potential to enhance sperm quality in assisted reproductive technology (ART).

Keywords: Cryopreservation, Asthenozoospermia, Papaverine, Acrosome reaction, Oxidative stress

P-8: Ketamine and Male Fertility: A Systematic Review

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Background: Ketamine (KET) has been known in human and veterinary medicine regarding its analgesic, anti-inflammatory, and anesthetic properties. Despite all medicinal advantages, the use of KET as a recreational drug has brought several concerns to public health. Accordingly, the adverse effects of KET on the nervous, cardiovascular, respiratory, and genitourinary systems have been reported previously, highlighting a great challenge considering the increasing abuse of KET worldwide.

Materials and Methods: This systematic review was conducted using international scientific databases, including Scopus, Google Scholar, MEDLINE, and Web of Science. The following keywords were used: ketamine, ketamine abuse, sperm, semen, testes, and male reproductive system. After reviewing 49 studies, 5 were excluded because their topics were not relevant. Finally, 32 articles were included in the review.

Results: Long-term use of KET can affect male reproductive health, leading to androgen imbalance, causing spermatogenic failure. Further, it is well-founded that KET abuse is involved in testicular oxidative injuries, testicular cell apoptosis, Sertoli cell dysfunction, and spermatozoa traits reduction and genetic disintegration. It has also been shown that KET decreases fertilizing potential through calcium signaling disturbance and plays a role in erectile dysfunction.

Conclusion: This study lays the groundwork for upcoming research to unveil the detailed KET abuse toxicities, particularly reproductive toxicity, and helps to increase public awareness about recreational drug abuse.

Keywords: Infertility, Ketamine, Male Reproductive Health, Substance Use Disorder

P-9: Association between Sperm DNA Fragmentation and Recurrent Implantation Failure

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Background: Recurrent implantation failure (RIF) is defined as the condition in which women experience three consecutive unsuccessful *in vitro* fertilization (IVF) attempts despite the transfer of good-quality embryos, with multiple contributing factors to its occurrence. Sperm DNA fragmentation (SDF) has emerged as a valuable tool for evaluating male fertility and can be a crucial factor for implantation failure. This study aims to investigate the relationship between sperm DNA fragmentation and unexplained RIF.

Materials and Methods: The current experimental study has been in progress since September 2024. Till now, sperm samples were collected from 8 men whose partner suffered from RIF as the RIF group and 15 fertile men who were referred to the Royan Institute for sex selection of the next child as the control group. Sperm morphology was measured by the Papanicolaou test, and sperm motility by the CASA method. The sperm DNA quality was assessed by the sperm chromatin dispersion (SCD) test and DFI were compared and analyzed using a t-test.

Results: Findings showed that sperm parameters such as morphology and motility did not have any significant differences between the RIF and control groups. DFI was significantly higher in the RIF group than in the control group ($20.81 \pm 9.12\%$ and $38 \pm 19\%$, respectively) ($P=0.0098$). A higher proportion of men with $DFI \geq 30\%$ was observed in the unexplained RIF population when compared to controls.

Conclusion: Our preliminary results suggest that sperm DNA fragmentation may be a crucial factor in RIF cases. The role of DFI as a predictive factor in assisted reproduction requires further investigation with larger sample sizes.

Keywords: *In Vitro* Fertilization, Recurrent Implantation Failure, DNA Fragmentation Index, Sperm

P-10: Microbial Dynamics of Semen: Impacts on Sperm Function and Male Infertility

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Background: Male reproductive health depends critically on the dynamic ecosystem, the seminal microbiome within semen, which shapes sperm quality and fertility. While traditionally thought of as sterile, semen contains a variety of microorganisms whose composition is influenced by both exogenous (such as sexual activity) and endogenous sources (such as the testes and prostate). Conditions, including prostatitis and HPV infection, as well as infertility and oxidative stress, are associated

with dysbiosis in this microbiome. The latest evidence on the origins, bacterial makeup, and links with male infertility of the seminal microbiome is synthesized in this systematic review.

Materials and Methods: This systematic search was conducted through Scopus, PubMed, and Science Direct, using keywords such as "semen microbiota," "male infertility," and "reproductive system health." After reviewing the studies, 40 studies were finally selected for the final evaluation, out of 626.

Results: Phyla ranging from Firmicutes to Proteobacteria, Actinobacteria, and Bacteroidetes make up the basic microbiome. While *Prevotella*, *Pseudomonas*, *Urea* plasma, and *Escherichia coli* are linked with lower fertility, sperm DNA fragmentation, and inflammation, genera such as *Lactobacillus* correlate with increased sperm motility and DNA integrity. Through partner exchange, sexual activity introduces a bacterial variety. Often accompanied by inflammation and oxidative stress, dysbiosis marked by decreased beneficial bacteria and increased pathogens is linked to male infertility and diseases, including HPV, chronic prostatitis, prostate cancer, and azoospermia.

Conclusion: Male fertility is strongly influenced by the basic microbiota; abnormalities cause oxidative stress and inflammation, which result in infertility. To resolve discrepancies, longitudinal studies and standardized research methodologies are essential. Targeted antibiotics and probiotics have the potential to help restore equilibrium. For research and clinical procedures to improve reproductive health, microbiome analysis must be incorporated into fertility assessments.

Keywords: Semen microbiota, Male infertility, Reproductive health

P-11: Effect of Rho kinase inhibitor (Y27632) on Apoptosis Status in Testicular Tissue of Azoospermic Mice

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Background: Advancements in cancer therapies that improve survival rates underscore the critical need for fertility preservation. The majority of cancer treatments induce apoptosis in rapidly dividing cells, including spermatogonial stem cells. Y27632, a selective Rho-associated protein kinase (ROCK) inhibitor, targets a crucial pathway involved in apoptosis during cellular stress conditions. This study investigates the impact of Y27632 on apoptosis-related gene expression and apoptosis status in busulfan treated mouse testicular tissue samples.

Materials and Methods: Eighteen 4-week-old male C57BL6 mice were divided into three groups: control, vehicle (busulfan 40 mg/kg), and treatment (busulfan 40 mg/kg + Y27632 5 mg/kg). The expression of apoptotic genes *Bax*, *Bcl2*, *Caspase3*, and *ERK*, as well as the average number of apoptotic-positive cells in testicular tissue as determined by the TUNEL test, were examined.

Results: Treatment with Y27632 showed a non-significant trend towards decreased pro-apoptotic gene expression (*Bax*, *Caspase3*) and increased anti-apoptotic gene expression (*Bcl2*) compared to the busulfan group. Notably, Y27632 significantly reduced *ERK* gene expression. The TUNEL assay showed that in the group treated with Y27632, the level of apoptosis was

significantly higher than in the control group ($P < 0.05$), but it was significantly lower compared to the group that received only busulfan ($P < 0.05$).

Conclusion: Administration of Y27632 in busulfan-treated mice resulted in a reduction in apoptotic gene expression and the number of apoptotic-positive cells. This suggests that Y27632 has potential as a component in therapeutic regimens for cancer patients to mitigate spermatogonia apoptosis following gonadotoxic treatments.

Keywords: Fertility, Cancer, Busulfan, Apoptosis, Y27632

P-12: Association between Sperm DNA Fragmentation and Semen Quality in Infertile Men: Role of Residual Histones and Inflammatory Marker IL-18

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Background: Male infertility is a multifactorial condition, and traditional semen analysis does not always reflect sperm functional integrity. Among advanced diagnostic tools, sperm DNA fragmentation (SDF) has gained attention as a potential indicator of fertility potential. Elevated SDF has been linked to poor reproductive outcomes, yet its association with conventional semen parameters, chromatin maturity, and inflammatory markers remains under investigation. This study aimed to assess the relationship between SDF levels and semen quality, chromatin integrity, and inflammation in infertile men.

Materials and Methods: This cross-sectional study included 60 infertile men categorized into two groups based on the Sperm Chromatin Structure Assay (SCSA): low SDF ($< 30\%$) and high SDF ($> 30\%$). Semen analysis was performed according to WHO guidelines, evaluating volume, sperm concentration, motility (total and progressive), viability, and morphology. Residual histone content was assessed using aniline blue staining. Interleukin-18 (IL-18) levels in sperm were measured as a marker of inflammation using ELISA method ($n=10$).

Results: There were no significant differences between the groups in semen volume ($P=0.3$) or total sperm count ($P=0.294$). However, men in the high SDF group showed significantly lower sperm concentration, total motility, progressive motility, and viability ($P < 0.05$). Sperm morphology was similar between groups. Aniline blue staining revealed a significantly higher proportion of immature chromatin (residual histones) in the high SDF group ($P < 0.01$). Additionally, IL-18 levels were elevated in the sperm of men with high DNA fragmentation ($P < 0.05$).

Conclusion: These results indicate that higher levels of SDF are associated with impaired semen quality, increased chromatin immaturity, and elevated inflammatory response, as evidenced by IL-18 levels. The findings highlight the potential role of SDF in the pathophysiology of male infertility and support the inclusion of DNA fragmentation and limited inflammatory profiling in the diagnostic evaluation of infertile men.

Keywords: Sperm DNA Fragmentation, Male Infertility, Semen

Analysis, Residual Histones, Interleukin-18

P-13: The Effect of Exosomes on Sperm Evaluation Parameters after Cryopreservation and Thawing

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Background: The process of sperm cryopreservation and thawing is associated with various damages, including reduced motility, disruption of the cell membrane, increased oxidative stress, and the induction of apoptosis and necrosis, ultimately leading to decreased fertility potential. Exosomes, a type of secreted extracellular vesicle ranging from 30 to 150 nanometers in size. These vesicles have been extracted from various animal sources such as seminal plasma, mesenchymal stem cells, and placenta, and have demonstrated significant roles in fertility processes and protection of sperm against cryo-injuries including oxidative stress, cell death, and membrane damage. A novel and less-explored area is the use of plant-derived exosomes, which, due to their natural antioxidant properties, may effectively reduce oxidative damage and sperm cell death. This study aims to evaluate the effect of plant-derived exosomes on sperm evaluation parameters following cryopreservation and thawing.

Materials and Methods: In this study, exosomes extracted from plants with high antioxidant capacities are added to the sperm extender. The sperm samples are then cryopreserved and, after thawing, analyzed. At this stage, key parameters including sperm motility, viability, and membrane integrity will be evaluated to assess the protective effect of exosomes on sperm quality.

Results: Preliminary findings from previous studies have shown that the addition of exosomes to sperm preservation media in veterinary and animal reproduction, particularly in species like pigs and cattle, consistently improves post-thaw sperm parameters. Our team is currently investigating the effects of both human- and plant-derived exosomes on human sperm quality.

Conclusion: Plant- and animal-derived exosomes, as biocompatible and effective additives, can play a significant role in improving sperm quality after cryopreservation. The use of these natural compounds offers a novel strategy for enhancing infertility treatments, increasing the success rate of assisted reproductive technologies, and expanding genetic resource banking in both medical and veterinary fields. Further research is required to identify the precise mechanisms of their action.

Keywords: Cryopreservation, Exosome, Extracellular-Vesicle

P-14: The Impacts of Hesperidin on Sperm Parameters and Biochemical Factors in Mice Treated With Titanium Dioxide Nanoparticles

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Background: The widespread application of nanoparticles, such as titanium dioxide (TiO_2), in daily products has raised concerns about their environmental and health impacts. High

doses of TiO₂ nanoparticles can accumulate in the testes, causing oxidative stress, inflammation, and potential organ damage due to their small size and high reactivity. These particles may disrupt the blood-testis barrier, leading to sperm abnormalities through oxidative stress pathways. This study aimed to investigate the effect of Hesperidin, an antioxidant found in the citrus family, on the sperm parameters and serum biochemical factors in mice treated with Titanium dioxide nanoparticles.

Materials and Methods: In this experimental study, twenty-four NMRI male mice were randomly divided into 4 groups: 1) control, 2) TiO₂- NPs (100 mg/kg BW/day), 3) Hesperidin (100 mg/kg BW/day), 4) TiO₂- NPs+ Hesperidin (100 mg/kg BW/day) and treated orally for 35 days. All animals were anesthetized with ketamine and xylazine, and the epididymides were excised and placed in Ham's F10 for sperm parameter analysis (count, motility, viability, and abnormality). In addition, stress oxidative markers, including lipid peroxidation (MDA level) and total antioxidant capacity (TAC) (FRAP test), were assessed in blood serum. Data were analyzed using One-way ANOVA and Tukey's test, and the means were considered significantly different at ($P<0.05$).

Results: The group treated with TiO₂- NPS showed a significant decrease in sperm count, motility, viability, and TAC level, and a significant increase in sperm abnormality and MDA level compared to the control group ($P<0.05$). The TiO₂- NPs+Hesperidin group exhibited a significant increase in the sperm parameters and TAC level and a significant decrease in MDA level compared to the TiO₂- NPs group ($P<0.05$).

Conclusion: The results of this study indicated that hesperidin ameliorated the adverse effects of TiO₂ nanoparticles on sperm parameters and oxidative stress markers in mice.

Keywords: Titanium Dioxide Nanoparticles, Hesperidin, Sperm, Oxidative Stress, Mice

P-15: Centrifuge-Free Microfluidic Sperm Selection: Enhanced Efficiency and Sperm DNA Integrity Compared to Conventional Methods

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Background: Conventional sperm preparation techniques (swim-up, density gradient centrifugation - DGC) necessitate centrifugation, prolonged processing (>60-90 minutes), and open handling. This poses significant risks of iatrogenic sperm DNA damage and exogenous contamination, potentially compromising assisted reproductive technology (ART) outcomes. To address these limitations, we evaluated a novel microfluidic sperm separation chip designed for rapid, specialist-independent, centrifuge-free selection within a fully closed system, thereby eliminating operator-dependent variability.

Materials and Methods: Over 50 clinical semen samples (normozoospermic, $n=32$; oligozoospermic, $n=19$) were processed using the single-step microfluidic chip. Comprehensive pre- and post-selection analysis assessed: Total Motility & Progressive Motility Viability (Eosin-Nigrosin staining) Morphology (Strict Kruger criteria) DNA Fragmentation Index (Sperm Chromatin Dispersion assay - SCD)

Results: The microfluidic chip significantly enriched high-quality sperm populations: Progressive Motility increased by $38.7\% \pm 8.2\%$ ($P<0.001$) Total Motility increased by $32.5\% \pm$

7.9% ($P<0.001$) Viability increased by $12.8\% \pm 4.3\%$ ($P<0.01$) Normal Morphology not significantly changed. Critically, DNA Fragmentation Indices (DFI) showed no statistically significant alteration (Pre: $16.3\% \pm 4.8\%$ vs. Post: $16.1\% \pm 4.6\%$; $P=0.42$), demonstrating absence of procedure-induced genetic damage. The closed-system design eradicated contamination risks. Processing was completed within 30 minutes without pre-treatment. Crucially, the specialist-independent operation ensured consistent outcomes irrespective of operator expertise. **Conclusion:** This microfluidic platform delivers rapid, standardized, and gentle sperm selection while robustly preserving DNA integrity – a critical determiner of IVF/ICSI success. The elimination of centrifugation, open handling, and complex protocols, combined with a fully enclosed workflow and operator-independent function, offers transformative practical, safety, and standardisation advantages over conventional techniques. This technology presents a compelling solution for modern ART laboratories seeking efficient, reproducible, and accessible sperm processing.

Keywords: Microfluidic Sperm Selection, Centrifuge-Free Sperm Processing, Sperm DNA Fragmentation Preservation, Operator-Independent ART

P-16: The Influence of Mental Health Disorders on Sperm Parameters: A Focus on Depression and Anxiety

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Background: Male infertility, affecting numerous couples globally, stems from diverse physiological and environmental causes, with growing evidence implicating psychological factors in reproductive impairment. Notably, depression and anxiety may negatively impact semen quality through biological pathways like elevated sperm DNA fragmentation (SDF), though comprehensive data linking mental health to specific sperm abnormalities remain limited. This study investigates the correlation between depression, anxiety, semen quality, and sperm DNA integrity in infertile men.

Materials and Methods: This observational cross-sectional study enrolled 110 infertile men aged 28 to 48 years attending the Fertility Center of Shahid Beheshti Hospital between April 2024 and March 2025. Psychological status was assessed using the standardized Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) questionnaires. Semen samples were collected via masturbation after 3–5 days of abstinence and analyzed according to WHO 10th edition guidelines. Evaluated parameters included sperm concentration (million/mL), total sperm count, motility (progressive and non-progressive), morphology (% normal forms), and viability. Sperm DNA fragmentation was measured using two complementary methods: Sperm Chromatin Structure Assay (SCSA) and TUNEL assay

Results: Depression severity demonstrated a robust negative correlation with multiple sperm parameters. Men with moderate-to-severe depression (BDI score ≥ 20) exhibited significantly lower sperm concentration, total sperm count, progressive motility, non-progressive motility, and normal morphology compared to men with minimal or no depression (all $P<0.05$). Furthermore, elevated SDF levels were significantly associated

with increased depression severity ($P < 0.05$). Anxiety levels, assessed by BAI, showed no significant association with most semen parameters or SDF, except for a modest but statistically significant reduction in sperm concentration.

Conclusion: The study reveals that depression significantly impairs sperm quality and DNA integrity, while anxiety shows minimal effects; these results emphasize the need for psychological assessment in male infertility management.

Keywords: Sperm DNA Fragmentation, Depression Anxiety, Semen Parameters, Male Infertility, Psychological Stress

P-17: An Integrative Study of Gene Expression Profile Fluctuation During Spermatogenesis Using ScRNA-Seq Data

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Background: Spermatogenesis is a tightly controlled process of the conversion of spermatogonia into spermatozoa under precise gene expression regulations. Recently, single-cell RNA sequencing has been considered a useful tool for capturing the gene expression profile within complex tissues and deciphering the developmental trajectory. Herein, we utilized scRNA-seq data to study the normal process of spermatogenesis and underscore key regulatory genes.

Materials and Methods: The raw reads of dataset GSE109037 were retrieved from the Sequence Read Archive (SRA), and count matrices were constructed following alignment and annotation. After normalization and integration, clustering was carried out using the KNN algorithm following the UMAP nonlinear dimensionality reduction. Following annotation with published cell type markers, differentially expressed genes (DEGs) were identified using the non-parametric Wilcoxon rank-sum test for each cluster, and enrichment analysis was performed. Trajectory analysis was performed using Monocle3, and DEGs were found alongside the pseudotime. Lastly, the Weighted Gene Co-expression Network Analysis (WGCNA) analysis was performed to show regulation modules, hub genes, and key genes using betweenness centrality (BC).

Results: Differentially expressed analysis in the 13 identified clusters revealed unique DEGs. The enrichment analysis highlighted highly activated pathways such as mitotic and meiotic processes in spermatogonia and spermatocytes, respectively. Pseudotime trajectory analysis supported the developmental progression suggested by clustering. Further characterization of spermatogonial cells showed two main subpopulations: one expressing stemness-associated genes like UTF1 and ID4, resembling the A cell types, and another expressing mitosis-promoting genes like DMRT1, consistent with B cell types. WGCNA analysis identified four gene expression modules, which correspond to distinct levels of differentiation. RPL18A, SPATA8, LYZ1, and C20orf141 emerged as top hub genes within modules enriched in spermatogonia, spermatocytes, early spermatids, and late spermatids, respectively. Furthermore, the ACTG1, CDKN1, and FAM229A were identified as the genes with the highest BC score.

Conclusion: In this study, we characterized the dynamic gene expression profile during the spermatogenesis process in healthy individuals. We also highlighted the key regulators that may have a critical role in the normal differentiation of sperm cells.

Keywords: Spermatogenesis, Male Fertility, scRNA-Seq

P-18: Molecular Characterization of Human Spermatogonial Stem Cells: Enrichment, Gene Expression Profiling, and Downregulation of Translocase of Outer Mitochondrial Membrane Genes and Machine Learning-Based Single-Cell Sequencing

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Background: Human spermatogonia stem cells (SSCs) are vital for spermatogenesis and hold potential for regenerative therapies and infertility treatment. This study aimed to enrich and characterize human SSCs through CD49f-based magnetic-activated cell sorting (MACS) and matrix-based selection (collagen non-binding/laminin-binding).

Materials and Methods: Isolated cells exhibited typical SSC morphology—small (6–12 μ m), spherical cells with high nucleus-to-cytoplasm ratios—and expressed key germline markers including DDX4, SSEA4, STELLA, and UTF1. Cultures showed spermatogonia pairs, chains, and clusters, while human fibroblasts (htFibs) were successfully depleted. Microarray analysis of 198 transporter genes identified 20 upregulated and 20 downregulated genes in SSCs versus fibroblasts.

Results: Notably, several genes related to the translocase of the outer and inner mitochondrial membrane (e.g., TOMM5, TOMM7, TOMM20, TIMM10, TIMM22) were significantly downregulated, suggesting altered mitochondrial import mechanisms in SSCs. Gene ontology and KEGG enrichment analyses revealed associations with telomere function, protein localization, and DNA biosynthesis regulation. Protein-protein interaction (PPI) and weighted gene co-expression network analysis (WGCNA) identified hub genes and functional modules associated with the cell cycle, ribosomal function, and metabolic pathways. Single-cell RNA sequencing of human testes across developmental stages mapped 17 cell clusters and revealed dynamic germ-somatic cell ratios during maturation.

Conclusion: These findings deepen our understanding of SSC-specific gene expression and mitochondrial dynamics, offering insights into male germline development and stem cell maintenance.

Keywords: Mitochondrial, Spermatogenesis, Translocase, Single-Cell RNA Sequencing

P-19: Oxidative Stress and Sperm Quality: An *In Vitro* Study on The Protective Role of Alpha-lipoic Acid on Cadmium-induced Toxicity in Human Spermatozoa

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Background: Cadmium is an environmental pollutant that negatively impairs male fertility. Its bioaccumulation in plants and aquatic organisms allows it to enter the human food chain, affecting human health. Epidemiological studies show a correlation between cadmium exposure and male infertility induced by oxidative stress. This study examines the effect of alpha-lipoic acid (ALA), a potent antioxidant, on oxidative stress markers and human sperm parameters treated with cadmium.

Materials and Methods: Human semen samples were washed with Ham's F10 and divided into 5 groups: 1) 0-hour group, 2) Control group, 3) Spermatozoa treated with cadmium chloride (10 μ m), 4) Spermatozoa treated with cadmium chloride (10 μ m) + ALA (50 μ m), and 5) Spermatozoa treated with ALA (50 μ m). Groups 2-5 were incubated at 37°C for 180 minutes. Vital sperm parameters (motility, viability, plasma membrane and acrosome integrity, mitochondrial membrane potential, and DNA fragmentation), and oxidative stress markers [(total antioxidant capacity (TAC) and malondialdehyde (MDA)] were assessed in the sperm samples.

Results: Cadmium significantly ($P < 0.001$) decreased sperm motility, viability, plasma membrane, acrosome, and DNA integrity, and mitochondrial membrane potential compared to the control group. Cadmium also significantly increased the level of MDA and decreased the TAC level compared to the control group. ALA significantly reversed the toxic effects of cadmium chloride on the sperm parameters compared to the cadmium group.

Conclusion: This study demonstrates that cadmium-induced toxicity in human vital sperm parameters is mediated by oxidative stress, and ALA, as a potent antioxidant, ameliorates the detrimental effects of cadmium. Exploring the efficacy of ALA in combination with other antioxidants may provide a more comprehensive approach to preserving male fertility in environments with cadmium exposure.

Keywords: Human Sperm, Cadmium Chloride, Alpha-Lipoic Acid, Oxidative Stress, Sperm Parameters

P-20: The Effect of Exosomes Extracted from PRP and Autologous PRP on Sperm Quality After Freezing and Thawing in Patients with Asthenoteratozoospermia

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Background: Infertility is one of the major challenges in today's societies that has affected millions of couples. According to the definition of the World Health Organization, infertility is known as the inability of couples to conceive after one year of regular, unprotected sexual intercourse. In this regard, clinicians and scientists recommend that people pay attention to fertility preservation. Fertility preservation in men is vital, and sperm freezing is an effective method in this regard, although it may have some side effects. This study investigates the effect of platelet-rich plasma (PRP) on the quality and viability of frozen sperm in men with asthenoteratozoospermia.

Materials and Methods: Semen collection of 45 men with asthenoteratozoospermia, who had been referred to the Infertility Center of Imam Reza Hospital, Mashhad for spermogram testing; divided into 3 groups: freezing without intervention

(Control, incubation with PRP one hour before freezing (PRP/Before) and incubation with PRP one hour after thawing (EXO/Before). Finally, sperm parameters, including motility, morphology, chromatin maturation, DNA fragmentation, and oxidative stress, were evaluated in all samples.

Results: In this study, it was observed that in the group that was incubated with exosomes before freezing (Exo/Before), sperm motility was higher than control and other groups. Also, the amount of DNA fragmentation and the level of oxidative stress in the Exo/Before group were significantly lower than other groups.

Conclusion: Based on the present study, incubating semen with PRP for about 1 hour before freezing does not affect sperm parameters; however, it improves the levels of indicators related to oxidative stress.

Keywords: Exosome, PRP, Sperm, Asthenozoospermia

P-21: Effects of Re-freezing and Double Thawing on Sperm Quality Parameters Following Freezing

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Background: Cryopreservation of human sperm is a valuable therapeutic option in male fertility management. This method is commonly used to preserve the fertility potential of male cancer patients before chemotherapy or radiotherapy. However, successful cryopreservation can be challenging in oligozoospermic patients due to the low sperm count in their ejaculate. When divided into aliquots, each aliquot contains only a small number of spermatozoa, further complicating the process. Therefore, this study aimed to evaluate the effects of re-freezing and double thawing on sperm quality parameters following cryopreservation.

Materials and Methods: A total of twenty semen samples were obtained after 3–5 days of sexual abstinence from normozoospermic men. This study consisted of two experiments. In the first experiment, frozen stored samples were thawed and refrozen without any further manipulation. In the second experiment, freshly frozen samples were thawed after one month (thawing 1 group) and six months (thawing 2 group) of storage in liquid nitrogen, and sperm parameters were evaluated.

Results: Sperm motility, viability, membrane integrity, and large halo rates of DNA damage decreased in the double freezing group. However, Sperm motility, large halo, and normal morphology rates decreased significantly in thawing 1 and 2 compared to fresh. There were no significant differences in sperm parameters between the first and second thawing intervals.

Conclusion: Our finding reveals that the interval of sperm thawing did not affect the sperm quality. Therefore, freezing semen samples in different aliquots and thawing them at different intervals is suitable for oligozoospermic samples that are at risk of azoospermia.

Keywords: Refreezing, Double Thawing, Sperm Parameters, Vittrification

P-22: Investigating The Effect of Cold Atmospheric Plasma on The Viability and Colony Quantification of Spermatogo-

nia Stem Cells

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Background: Male infertility is a major public health issue, contributing to approximately 50% of infertility cases. Spermatogonia stem cells (SSCs) are specialized cells located in the testicular seminiferous tubules, responsible for initiating and maintaining spermatogenesis, and damage or dysfunction of these cells can disrupt spermatogenesis and lead to infertility. Cold atmospheric plasma (CAP) is a partially ionized gas produced at room temperature and atmospheric pressure. CAP consists of a mixture of reactive oxygen and nitrogen species (RONS), nitric oxide (NO), ultraviolet radiation, and electric fields. These components, at moderate levels, can activate key signaling pathways such as PI3K/AKT and ERK, thereby promoting the proliferation and survival of stem cells. However, exposure to high-intensity CAP may cause DNA damage and induce apoptotic pathways.

Materials and Methods: In this study, rat neonate SSCs were isolated, cultured in 96-well plates, and treated with CAP.

Results: The results of the MTT test showed that treatment with a plasma jet with technical specifications including a voltage of 14 kV, a frequency of 14 kHz, and a helium gas flow rate of 1 SLM had the greatest increase in cell viability and colony count compared to the control.

Conclusion: These findings suggest that CAP, under carefully controlled conditions, can serve as a non-invasive tool for enhancing the viability of spermatogonia stem cells. Nevertheless, precise optimization of plasma parameters is essential to avoid potential cytotoxic effects.

Keywords: Cold Atmospheric Plasma, Spermatogonia Stem Cells, Viability, Male Infertility, Plasma Jet

P-23: The Effects of Adding Plasma-Rich Growth Factors in Different Stages of Freezing on Sperm Parameters in Normozoospermic and Asthenoteratozoospermic Samples

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Background: Sperm cryopreservation is an effective method used in infertility treatment centers. However, this method may have detrimental effects, including decreased sperm quality after freezing and thawing. In this study, the effects of plasma-rich in growth factors (PRGF) at different stages of cryopreservation on sperm parameters in normal and asthenoterato samples were evaluated.

Materials and Methods: This study was conducted in two stages. In the first stage, 20 normal semen samples were included in the study. After preparation, the spermatozoa were divided into the following groups: a control group that was frozen and thawed without 1% PRGF, and three groups that received 1% PRGF before equilibration, during equilibration, and after thawing. The rapid freezing method was used to freeze the

sperm samples. Sperm motility, viability, normal morphology, DNA fragmentation, reactive oxygen species (ROS) levels, and mitochondrial membrane potential were evaluated in different groups before freezing and after thawing. Based on the results of the first stage, to select the appropriate time for adding 1% PRGF, in the second stage, 1% PRGF was added to ten asthenoterato samples and the parameters were evaluated as in the first stage and compared with the control group (without 1% PRGF).

Results: Progressive motility in all groups was significantly reduced compared to before freezing. Also, in the freezing group, the total motility and viability parameters increased significantly compared to the control group. The rate of DNA fragmentation also increased significantly in all groups, except the during freezing group. In the second stage, the group that received 1% PRGF did not differ significantly compared to the pre-freezing group for the total motility, viability, and DNA integrity, while significant differences were observed in the control group for total sperm motility parameters, viability, and DNA integrity.

Conclusion: Adding 1% PRGF to the freezing medium during the freezing process yields effective results. PRGF effectively preserves sperm motility, viability, and DNA integrity in asthenoterato samples.

Keywords: Sperm, Freezing, Thawing, PRGF

P-24: Evaluation of Acute and Chronic Phases of COVID-19 on Semen Parameters and Gonadotropin Hormones: A Case-Control Study

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Background: Since the outbreak of COVID-19, increased studies have proved that it has an impact on the male reproductive system. This study aimed to investigate the effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on various aspects of male reproductive function.

Materials and Methods: This case-control study was conducted on seventy men at Ganjovian Dezful Hospital, Dezful, Iran, from July 2022 until January 2023. Participants were divided into COVID-19-positive (n=35) and negative groups (n=35). Semen samples were collected during the acute and chronic phases. Semen parameters, SARS-CoV-2 detection, oxidative stress markers, and sex hormones were evaluated.

Results: The study found significant differences in semen parameters, including motility (P<0.001), progressive motility (P<0.001), and normal morphology (P=0.001), between COVID-19-positive and negative groups, as well as within the COVID-19-positive group between the acute and chronic phases. Sperm motility was significantly reduced during the acute phase compared to the chronic phase in the COVID-19-positive group (P<0.001), suggesting early impairment with some re-

covery over time. The COVID-19-positive group also showed significant differences in follicle-stimulating hormone, luteinizing hormone, and oxidative stress markers ($P < 0.001$) compared to the negative group. However, SARS-CoV-2 RNA was not detected in any of the semen samples.

Conclusion: The Omicron variant of SARS-CoV-2 infection in vaccinated men was associated with transient impairment of semen quality, increased oxidative stress, and secondary hypogonadism during the acute phase. These findings highlight the potential impact of COVID-19 on male reproductive health and the importance of further research to understand the long-term effects of different SARS-CoV-2 variants.

Keywords: Gonadotropin Hormones, Oxidative Stress, SARS-CoV-2, Semen Analysis

P-25: Investigating The Relationship between SPAM1 Gene Expression in Sperm and IUI Outcome

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Background: A common and effective treatment for couples with unexplained or mild male factor infertility is intrauterine insemination (IUI). In IUI, sperm surface proteins play a crucial role in sperm-oocyte interaction and fertilization. Specific proteins like sperm adhesion molecule 1 (SPAM1) participate in this process, and variations in their expression or function can impact IUI success. SPAM1 protein on the sperm head plays a key role in sperm penetration into the hyaluronic acid-rich matrix surrounding the oocyte. This study aims to investigate the gene expression of SPAM1 in the sperms of men whose partners are undergoing IUI cycles.

Materials and Methods: Semen samples from 300 men (Age ≤ 45 years old, BMI ≤ 30 Kg/m²) whose wives undergo IUI cycles at Royan Institute will be included in this cohort study. According to the IUI outcome, 30 IUI successes and 30 failed IUI samples will be studied. Up to now, the remaining semen samples of twelve men were collected from the Royan embryology laboratory on the day of IUI. After sperm separation, RNA extraction was performed using the Kiazol, and cDNA synthesis was done using the SMOBio kit. The gene expression level of the SPAM1 was examined in comparison with β -actin as a housekeeping gene using Real-time RT-PCR. Data analysis was done using SPSS and T t-test.

Results: The preliminary finding showed that gene expression of SPAM1 in sperm had no significant difference between the IUI failed and IUI success groups.

Conclusion: According to the current result, there is no association between SPAM1 gene expression level in sperm and IUI success rate. The definitive conclusion will be drawn after col-

lecting all samples.

Keywords: Infertility, IUI, SPAM1, Sperm, Gene Extraction

P-26: The Small Molecule Y-27623 Improves Sperm Quality Parameters After The Vitrification Process

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Background: Controlling apoptosis is crucial during sperm freezing. Sperm vitrification, a rapid freezing technique employing high cryoprotectant concentrations, is one such method. Compound Y-27623, a small molecule with anti-apoptotic properties, can modulate apoptotic pathways. This study aims to evaluate the impact of varying concentrations of Y-27623 added to the vitrification medium on sperm quality post-thaw.

Materials and Methods: Following initial qualitative analysis of a human sperm sample, the sample was divided into equal concentrations in freezing media and treated with Y-27623 at concentrations of 5, 10, and 20 μ M. After vitrification and thawing, sperm motility, viability, plasma membrane integrity, acrosome integrity, and DNA fragmentation were assessed.

Results: The results indicated that the lower concentration (5 μ M) of Y-27623 led to significant improvements in sperm total and progressive motility, viability, and plasma membrane integrity compared to the control group ($P < 0.05$). But in DNA fragmentation index, there is not remarkably differences between treatment and control group

Conclusion: These observations suggest that Y-27623 component at lower dosage (5 μ M) more effective at enhancing post-thaw sperm quality factors.

Keywords: Y-27623, Vitrification, Apoptosis, Sperm

P-27: Effects of Ellagic Acid Supplementation in Vitrification Solution on Human Sperm Quality Following Warming

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Background: Sperm cryopreservation is an essential technique for fertility preservation in men. However, conventional slow freezing often leads to cellular damage due to ice crystal formation. Vitrification prevents ice formation by solidifying cells into a glass-like state, thereby better preserving sperm motility and DNA integrity. Ellagic acid, as a polyphenolic antioxidant, has shown potential in protecting sperm during freezing. There-

fore, this study aims to evaluate the efficacy of adding ellagic acid to the vitrification solution of sperm quality following cryopreservation.

Materials and Methods: The semen samples of twenty men were collected after 3-7 days of sexual abstinence. After primary evaluation, semen samples were processed by swim up and diluted in vitrification solution containing 0, 0.1, and 1 M ellagic acid. After that samples were vitrified directly in liquid nitrogen. After 7-day storage in liquid nitrogen, the samples were thawed and sperm parameters, including total motility, progressive motility, membrane integrity, viability, and DNA integrity, were assessed.

Results: Sperm motion characteristics and membrane integrity were significantly higher in 1 M ellagic acid compared to the control group ($P < 0.05$). However, no statistically significant differences were seen in the percentage of viable sperm following vitrification. According to DNA integrity results, supplementation of vitrification solution with 1 M ellagic acid showed significantly higher percent of large halo cells compared to the control group.

Conclusion: Our study showed that supplementation of vitrification solution with 1 M ellagic acid could increase the quality of human spermatozoa following the freeze-thaw process.

Keywords: Vitrification, Ellagic Acid, Post-Thaw Quality, Human Sperm

P-28: The Effects of Oral Vitamin D3 Administration on Canine Fresh and Frozen-Thawed Spermatozoa Quality Measures

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Background: Vitamin D3 is widely used due to common deficiency in the population. However, its effect on healthy animals remains unclear. This study aimed to assess how vitamin D3 affects fresh and frozen-thawed sperm quality in healthy male dogs.

Materials and Methods: The treatment group ($n=4$) received 1000 IU of orally vitamin D3 daily, for two months, the control group ($n=4$) got a placebo. Semen was collected bi-weekly, assessed fresh, and cryopreserved for later tests. Fresh and frozen-thawed sperm were evaluated for motility, viability, and membrane, acrosomal and DNA integrity.

Results: Vitamin D3 had no significant effect on motility parameters in fresh sperm. DNA integrity of fresh sperm increased in both treatment and control groups over time, however significant differences were only observed on Day 14. A significant increase in DNA integrity was seen in the treatment group only on Day 14 compared to baseline. Treatment had no effect on fresh sperm viability, membrane, or acrosome integrity. Most frozen-thawed sperm parameters, including kinematics, showed no change. However, treatment group showed a significant improvement in progressive motility on Day 42 and Day 56, as compared baseline frozen-thawed sperm. No other qualities changed significantly with treatment.

Conclusion: Daily vitamin D3 slightly improved sperm motility and DNA integrity in healthy dogs. Interestingly, even though the dogs were healthy and not vitamin D deficient, the administration of 1000 IU/day still resulted in some observable

enhancements. Thus, concerns about antioxidant overuse may not apply to vitamin D3, though more studies are needed to define safe limits.

Keywords: Fertility, Oxidative Stress, Sperm, Vitamin D3

P-29: The Effect of Theobromine on The Expression of Apoptosis-Related Genes During Sperm Cryopreservation in Infertile Men with Asthenozoospermia

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Background: Asthenozoospermia is characterized by reduced sperm motility, which can lead to male infertility. Sperm cryopreservation, commonly used in assisted reproductive techniques, often causes considerable damage to sperm quality. The addition of antioxidants to the cryopreservation medium may help mitigate the adverse effects of the freezing process. Theobromine (TB), a plant-derived alkaloid belonging to the methylxanthine family, is widely recognized for its antioxidant properties and potential protective effects. The aim was to investigate the effects of theobromine on the expression of apoptotic and anti-apoptotic genes in cryopreserved sperm from asthenozoospermic men.

Materials and Methods: thirty semen samples were collected from Asthenozoospermic patients. Each sample was divided into three groups: Control (fresh), Freeze (treated with cryoprotectant), and Freeze+ TB (treated with cryoprotectant and 10 mmol/L theobromine). Cryopreservation was performed through the rapid freezing method. In each sample, the expression of the genes *Bax*, *Bcl2* and *Caspase 3*, were analyzed using Real-time PCR. The results were reported as fold change ($\Delta\Delta C_t$ formula). Data were analyzed statistically using Repeated Measure Analysis and Bonferroni post-hoc test.

Results: The expression levels of *Bax* and *Caspase 3* genes in the freezing group were significantly increased compared to the control group ($P < 0.001$), while the expression level of *Bcl2* gene did not change significantly ($P > 0.05$). Also, the expression levels of and *Caspase 3* genes in the freezing + TB group were not significantly changed compared to the freezing group ($P < 0.001$), while the expression level of *Bcl2* gene decreased significantly ($P < 0.001$).

Conclusion: Our data show that the addition of TB to the sperm freezing medium does not affect the expression of *Bax* and *Caspase-3* genes, but significantly reduces the expression of the *Bcl2* gene.

Keywords: Asthenozoospermia, Cryopreservation, Gene Expression, Theobromine,

P-30: Ameliorative Effects of Citrus Aurantium on Arsenic-Induced Testicular Toxicity in Male Rats

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Background: Heavy metals exert their toxic effects on male reproduction by causing oxidative stress. Citrus aurantium: The present study was done to investigate whether the ethanolic extract of Citrus aurantium could protect male rats against arsenic-induced testicular oxidative stress.

Materials and Methods: In this experimental study, adult Wistar rats were treated with arsenite sodium (100 ppm) in drinking water alone or with 50, 100, or 200 mg/kg body weight of Citrus aurantium extract via gavage once daily for 70 days. The weight of their reproductive organs, levels of serum hormones, histometric parameters of the seminiferous tubules and oxidative stress status were evaluated.

Results: The testis weight, seminiferous tubule diameter, serum testosterone level, and testicular levels of superoxide dismutase and glutathione peroxidase were significantly reduced ($P<0.05$) in the arsenic-treated rats. Moreover, significantly ($P<0.05$) higher levels of malondialdehyde were observed in the arsenic-exposed group compared to the control. However, reproductive parameters were improved significantly in the arsenic-treated rats co-administered with Citrus aurantium extract.

Conclusion: Our results showed that Citrus aurantium extract has the potential to prevent oxidative toxicity induced by arsenic and to suppress the adverse effects of arsenic on male reproductive health.

Keywords: Citrus Aurantium, Arsenite Sodium, Oxidative Stress, Reproductive Health

P-31: Effects of L-Carnitine Over-Supplementation on Sperm Function in Healthy NMRI Mice

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Background: L-carnitine (LC) is a pivotal regulator of lipid metabolism, facilitating the transport of long-chain fatty acids into mitochondria for β -oxidation and energy production. Beyond its metabolic role, LC possesses notable antioxidant, anti-inflammatory, and anti-apoptotic properties, contributing to cellular protection and homeostasis. This study aimed to evaluate the potential detrimental effects of excessive LC supplementation on sperm function in healthy NMRI male mice.

Materials and Methods: Mice were administered LC at doses of 20 and 500 mg/kg body weight daily for four weeks ($n = 6$ per group). Sperm parameters—including motility, concentration, and morphology—were evaluated, alongside assessments of sperm chromatin and DNA integrity using Aniline Blue (histone retention), Chromomycin A3 (protamine deficiency), and Acridine Orange (DNA fragmentation) staining methods. Liver tissues were fixed and H&E-stained for histological analysis.

Results: After four weeks, the high-dose LC group (LC500) exhibited a significant increase in liver weight compared to controls ($P<0.05$). Although sperm parameters remained unchanged across groups, the LC500 group showed a significant reduction in sperm chromatin and DNA integrity ($P<0.05$). Histological examination of liver tissues from LC500-treated mice revealed substantial lipid droplet accumulation, contrasting with the normal hepatic architecture observed in controls.

Conclusion: These findings suggest that while LC is essential for energy metabolism, excessive supplementation may adversely affect male reproductive health by inducing sperm chromatin damage and DNA fragmentation. Additionally, prolonged high-dose LC intake may promote hepatic lipid accumulation and inflammation, implicating a potential risk for non-alcoholic fatty liver disease (NAFLD). Careful consideration of LC dosage is therefore warranted to mitigate possible reproductive and hepatic complications.

Keywords: L-Carnitine, Over-Supplementation, Spermatozoa, DNA Fragmentation

P-32: Detailed Analysis of Sperm Cryopreservation and Its Impact on Chromatin Integrity

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Background: The effects of sperm freezing on chromatin integrity, oxidative damage, osmotic stress, and apoptosis while analyzing different freezing techniques and their effects are so controversial. The results therefore suggest that cryopreservation has profound effects on DNA integrity, chromatin stability and mitochondrial function, which results in poor fertility outcome and reduced success rate of assisted reproductive technologies.

Materials and Methods: The systematic review article was written using various databases, such as PubMed, Scopus, and Web of Science.

Results: Mechanisms of Cryoinjury in Sperm: 1. The Effects of ROS and Oxidative Stress: • Reactive Oxygen Species (ROS) cause the breakdown of DNA, shortening of chromatin, and reduction in sperm's motility during freezing. • ROS-rich spermatozoa pose severe risks to chromatin and the vitality of sperm, which reduces spermatozoa vitality. 2. Apoptosis: • In case there is physiological strain associated with freezing and osmotic disparities, the respective pathways to apoptosis get activated. 3. Osmotic Stress and Membrane Damage: • Cryopreservation disrupts the osmotic equilibrium of sperm cells, causing an outward stochastic movement of water from the cytoplasm, weakening the membrane's integrity. • Membrane damage results in a decrease in membrane permeability. Strategies for reducing Cryoinjury Effects: -natural antioxidants such as glutathione, vitamin E, and catalase may lessen damage because of oxidative stress. -There may also be preservation of chromatin structure, which allows optimal refinement of parameters such as freezing rate and addition of protective media into the freezing methods. -More effective identification of some sensitivity markers to cryoinjury in sperm cells is essential to be able to conserve fertility. -Constructive shielding nanoparticles may be able to enhance chromatin stability in sperm cells during cryopreservation.

Conclusion: Developing innovative cryopreservation techniques is essential for minimizing sperm chromatin damage. This involves reducing physiological stress, designing advanced protective systems, and optimizing storage conditions to improve pregnancy success in assisted reproduction.

Keywords: Sperm, Cryopreservation, Chromatin-Integrity

P-33: The Effect of Melatonin Nanoparticles on DNA, Chromatin, and Free Radical Levels in Men with Normospermia

After Rapid Freeze Cryopreservation

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Background: Male infertility is a significant concern, and sperm cryopreservation offers a solution for fertility preservation. However, freezing can damage sperm, reducing fertilization potential due to physical stress and oxidative damage. Melatonin, an antioxidant, may mitigate these effects, and nanoparticle technology could enhance its effectiveness.

Materials and Methods: In the above study, twenty normospermia samples from men referred to the Yazd Institute of Reproductive Sciences were used. Melatonin nanoparticles were synthesized using PEG6000, with size and zeta potential measured via DLS. Nanoparticles at concentrations of 1, 0.1, and 0.01 mg were added to the freezing medium, and samples were rapidly frozen. After one week, sperm parameters were assessed in terms of motility, morphology, protamine deficiency, and DNA fragmentation. A malondialdehyde kit was used to evaluate the ROS level.

Results: The results of the nanoparticle synthesis show that our melatonin nanoparticles have a size of 83.3 nm and a zeta size of -58.5 mV. Our results showed that 1 mg of melatonin nanoparticles added to the human semen freezing medium compared to other doses significantly improved the motility (21.60 ± 8.91), viability (44.25 ± 14.39), DNA fragmentation (10.00 ± 3.68), protamine deficiency (10.00 ± 3.68), and intracellular MDA (0.54 ± 0.05) concentration of sperm after thawing compared to the control group and consequently sperm fertilization ($P < 0.05$).

Conclusion: Sperm freezing can reduce the fertility potential. To our knowledge, this is the first report to investigate the protective effect of several concentrations of melatonin nanoparticles during human semen cryopreservation. Nanoparticles show promise as effective agents for delivering antioxidants like melatonin, enhancing sperm cryopreservation outcomes.

Keywords: Rapid Freezing, Nanoparticle, Melatonin, DNA/Chromatin Integrity, Free Radical

P-34: Evaluation of Microdeletions in The AZF Region of The Y Chromosome and Their Role in The Occurrence of Non-Obstructive Azoospermia

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Background: Non-obstructive azoospermia (NOA) is considered one of the most advanced manifestations of male infertility, often rooted in genetic abnormalities. Microscopic deletions in the Azoospermia Factor (AZF) region located on the Y chromosome (Yq11) are recognized as one of the most important known genetic causes in men with NOA. The AZF region is divided into three functional subregions: AZFa, AZFb, and AZFc; deleting each can create distinct patterns of spermatogenesis disruption.

Materials and Methods: In this review, studies related to

the topic up to 2024 were identified through a comprehensive search in the PubMed, Scopus, and Web of Science databases. The search was conducted using keywords such as "non-obstructive azoospermia," "Y chromosome," and "microdeletions in the AZF region." The selected studies evaluated microdeletions in different sections of the AZF region of the Y chromosome in patients with non-obstructive azoospermia.

Results: The global prevalence of Yq microdeletions among infertile men is reported to be around 7.5%, which is significantly higher in Asian populations. Most of the studies reported AZFc as the subregion with the highest deletion rate, which is associated with a range of spermatogenic disorders from oligozoospermia to azoospermia. AZFa deletions were associated with Sertoli cell-only syndrome, while AZFb deletions were usually associated with meiotic arrest. This difference between them indicates that genetic diversity in the structure of the Y chromosome includes diversity in several gene unit repeats and diversity in the genetic composition of the Y chromosome.

Conclusion: Microdeletions in the AZF region, especially AZFc, are an important genetic factor in NOA. Given the ability to transfer Yq deletions through assisted reproductive techniques to subsequent generations, genetic screening for infertility is of significant importance. In general, the identification and precise analysis of deletions in the AZF region can contribute to a better understanding of the molecular mechanisms of male infertility and play a key role in selecting effective treatment strategies.

Keywords: Male Infertility, Non-Obstructive Azoospermia, Yq Microdeletions

P-35: The Effects of Fluoxetine on Sperm Quality and Antioxidant Enzyme in Healthy Men: An *In Vitro* Study

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Background: Fluoxetine is one of the most prescribed selective serotonin reuptake inhibitors (SSRIs), widely used to treat depression and anxiety disorders. However, its potential impact on the male reproductive system warrants careful investigation. Emerging evidence suggests that fluoxetine can induce oxidative stress in various cell types, including ovarian epithelial and hippocampal cells. Given the frequent and long-term use of fluoxetine among men of reproductive age, it is particularly important to evaluate its effects on sperm cells *in vitro*.

Materials and Methods: Semen samples were collected from thirty fertile men. Each sample was divided into three groups: Fresh group analyzed immediately without any treatment; Control group incubated at 37°C for 1 hour without treatment; and Fluoxetine group treated with 5 µm fluoxetine and incubated under the same conditions for 1 hour. In all groups, the parameters including progressive motility, non-progressive motility, total motility, and sperm viability were evaluated. Additionally, levels of catalase (CAT), glutathione (GSH), superoxide dismutase (SOD), and reactive oxygen species (ROS) were measured. Data were analyzed using repeated measures analysis.

Results: The mean percentage of total and progressive motility and sperm viability, CAT, Glu and SOD levels in the fluoxetine group showed a significant decrease compared to the fresh and control groups ($P < 0.001$). While the mean percentage of non-

progressive motility and ROS in the fluoxetine group was significantly increased compared to the fresh and control groups ($P<0.001$).

Conclusion: The findings of the present study indicated that fluoxetine at 5 μM impairs sperm quality by reducing motility, viability, and antioxidant enzyme levels while increasing oxidative stress. These effects may impact male fertility, highlighting the need for further research on fluoxetine's reproductive risks.

Keywords: Fluoxetine, Human Sperm Parameters, Antioxidant Enzyme

P-36: In Vitro Effects of N-Acetylcysteine on The Quality and The Antioxidant Defense System of Normal Human Sperm

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Background: Infertility affects many couples and has led to increased use of assisted reproductive techniques (ART). Sperm processing, a key step in ART, can cause oxidative stress and reduce sperm quality. Antioxidants like N-acetylcysteine (NAC) may help protect sperm by neutralizing free radicals. This study investigates the effects of NAC on sperm quality, antioxidant defenses, and reactive oxygen species (ROS) levels in normal sperm during one hour of in vitro incubation.

Materials and Methods: After collection and complete liquefaction, semen samples from 30 healthy, fertile men were divided into two experimental groups. The first group served as the control (no treatment, 1-hour incubation), and the second group was treated with NAC (50 μM NAC, 1-hour incubation). At the end of the incubation period, both groups were evaluated for sperm motility and viability, along with levels of key antioxidant enzymes catalase (CAT), glutathione (Glu), and superoxide dismutase (SOD), as well as ROS levels. Data were analyzed using the repeated measures analysis method, and significant differences were considered at the $P<0.05$ level.

Results: In the NAC-treated group, the mean percentages of total and progressive sperm motility, DNA integrity, and the levels of antioxidant enzymes CAT, Glu, and SOD were significantly higher compared to the control group ($P<0.001$). Conversely, the mean percentage of non-progressive sperm motility and ROS levels were significantly lower in the NAC group than in the control group ($P<0.001$).

Conclusion: This study demonstrated that short-term in vitro treatment with NAC significantly improves sperm quality in healthy and fertile men by enhancing motility, DNA integrity, and antioxidant enzyme activity, while reducing oxidative stress, highlighting its potential role in assisted reproductive techniques to support sperm function

Keywords: Oxidative Stress, N-Acetyl Cysteine, Sperm Quality

P-37: Sperm Selection at $\times 400$ Magnification Cannot Improve Telomere Length of Selected Spermatozoa in Patients with Severe Teratozoospermia

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Background: Sperm selection from the population of processed spermatozoa cells after Density Gradient Centrifugation (DGC) can assist embryologists in selecting high-quality sperm. Sperm selection of low-quality and chromatin-damaged spermatozoa is inevitable in severe teratozoospermic semen specimens. This study was conducted to evaluate whether sperm selection at $\times 400$ magnification enables embryologists to select a population of spermatozoa with low DNA fragmentation and high sperm telomere length (STL) in semen samples with severe teratozoospermia.

Materials and Methods: A total of 23 infertile men characterized by severe teratozoospermia were selected. Sperm DNA fragmentation (SDF) and relative STL (r-STL) were evaluated at three stages: Specimen collection, after DGC, and during the single selection of spermatozoa at $\times 400$ magnification (single selection). The 23 patients were divided into two groups, including 14 with normal morphology $\leq 1\%$ and nine with normal morphology of 2%. SDF and r-STL were compared between the two groups at three stages.

Results: The results of this study showed that although SDF decreased remarkably after DGC and single selection ($F=64.327$, $P=0.000$), the DNA fragmentation index obtained for each semen sample was more than the cut-off point of 18% based on Halo sperm test. No statistically significant differences were observed in r-STL after DGC and single selection ($F=1.978$, $P=0.163$). Meanwhile, the pairwise comparison of r-STL showed that in the 2% normal morphology group, the mean relative telomere length was significantly higher in the selected spermatozoa compared to semen specimen ($P=0.014$). This increase can be attributed to DGC and single selection by the embryologist. Also, there was no correlation between SDF and r-STL in the semen samples with severe teratozoospermia ($r=0.01$, $P=0.964$).

Conclusion: This study suggests that while investing more time in sperm selection can decrease SDF, but r-STL of spermatozoa selected by the embryologist does not increase in severe teratozoospermia semen samples with morphology $\leq 1\%$.

Keywords: Density Gradient Centrifugation, DNA Fragmentation, Spermatozoa, Telomere, Teratozoospermia

P-38: The Effect of Theophylline on Sperm Biochemical Factors in Asthenozoospermic Men during the Freeze-Thaw Process

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Background: Asthenozoospermia (AZS), characterized by diminished sperm motility, represents a prevalent etiology of male infertility with multifactorial origins. While sperm cryo-

preservation serves as a critical component of assisted reproductive technologies (ART), the freeze-thaw process induces excessive reactive oxygen species (ROS) generation, compromising sperm quality. This study evaluates the protective effects of theophylline - a phosphodiesterase (PDE) inhibitor exhibiting anti-inflammatory properties - on biochemical parameters during cryopreservation in asthenozoospermic men.

Materials and Methods: Thirty semen samples were collected from men with asthenozoospermia referred to the Roya Infertility Treatment Center in Qom, Iran. Each semen sample was divided into three experimental groups: the control group (fresh sample), the freeze group (exposed to sperm freezing medium only), and the freeze + Theophylline group (treated with 0.05 mM theophylline). The levels of tumor necrosis factor alpha (TNF- α), interleukin-10 (IL-10), malondialdehyde (MDA), and antioxidant enzymes—superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX)—and total antioxidant capacity (TAC) were measured using the ELISA method.

Results: The results showed a significant increase in TNF- α and MDA levels and a significant decrease in antioxidant enzyme activity and IL-10 levels in the freezing group compared to the control group ($P < 0.05$). In contrast, a significant increase in the mean level of antioxidant enzymes and IL-10 and a significant decrease in MDA and TNF- α levels were observed in the freezing + theophylline group compared to the freezing group ($P < 0.05$).

Conclusion: Our results suggest that the addition of theophylline to sperm cryopreservation media improves the biochemical profile and modulates inflammatory markers by reducing ROS in asthenozoospermic men.

Keywords: Asthenozoospermia, Cryopreservation, Biochemical Parameters, Theophylline

P-39: Beneficial Effects of Selenium on Sperm Oxidative Stress and Inflammatory Factors in Asthenozoospermic Men During Cryopreservation

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Background: Cryopreservation of human sperm is a fundamental technique in reproductive medicine. Extensive research has explored the protective role of antioxidants in cryopreservation, particularly their ability to enhance post-thaw semen quality. Selenium, a vital trace element, supports male reproductive health by strengthening antioxidant defenses, improving sperm parameters, and mitigating oxidative stress. This study aims to evaluate the impact of selenium on biochemical markers in sperm from asthenozoospermic men during freeze-thaw cycles.

Materials and Methods: Semen samples were collected from thirty asthenozoospermic men at the Roya Infertility Treatment Center in Qom. Each sample was divided into three groups: (1) Control (fresh semen), (2) Freeze (sperm frozen in standard medium), and (3) Freeze + Selenium (sperm frozen in medium supplemented with 2 μ g/mL selenium). Levels of tumor necrosis factor-alpha (TNF- α), interleukin-10 (IL-10), malondialdehyde (MDA), and antioxidant enzymes—superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPX)—along with total antioxidant capacity (TAC), were assessed via

ELISA.

Results: Compared to the control group, the Freeze group exhibited a significant increase in TNF- α and MDA levels, alongside a marked decline in antioxidant enzymes and IL-10 ($P < 0.05$). In contrast, the Freeze + Selenium group demonstrated a significant rise in antioxidant enzymes and IL-10, coupled with a reduction in MDA and TNF- α levels relative to the Freeze group ($P < 0.05$).

Conclusion: Supplementing cryopreservation media with selenium appears to alleviate cryodamage, significantly enhancing antioxidant enzyme activity while reducing oxidative and inflammatory markers (MDA and TNF- α). These findings suggest that selenium may play a protective role in preserving sperm quality during freeze-thaw processes.

Keywords: Asthenozoospermia, Cryopreservation, Biochemical Parameters, Selenium

P-40: Microfluidic-Based Cryopreservation of Normal Human Spermatozoa

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Background: Sperm cryopreservation is a technique for preserving male fertility, which can cause significant damage to sperm cells, due to ice crystal formation, osmotic stress, and membrane disruption, affecting sperm viability, motility, and fertilization potential. Microfluidics may offer promising approaches to minimize these effects as it allows for gradual mixing of the cryoprotectant agent (CPA) and sperm sample over time, hence improving sperm parameters after freezing-thawing. In this study, we reduced cell damage by designing a new micromixer-based chip for sperm cryopreservation. We compared sperm parameters before and after the freezing-thawing process.

Materials and Methods: In this study, 20 semen samples with normal sperm parameters were collected. An initial evaluation was conducted, and the samples were prepared using the swim-up method. Parameters such as viability, total motility, progressive motility, normal morphology, DNA integrity, and mitochondrial membrane potential (MMP) were analyzed before freezing. The samples were divided into conventional equilibration and microfluidics equilibration groups to achieve equilibrium with CPA. Then, the samples were cryopreserved using a rapid freezing method. After thawing, all parameters in both groups were evaluated and compared to parameters before freezing.

Results: The results obtained in this study showed that viability, total motility, and MMP significantly increased in the microfluidics equilibration group compared to the conventional equilibration group. The sperm viability in the groups before freezing, conventional equilibration, and microfluidics equilibration groups was, respectively 90 ± 6.3 , 63.78 ± 10.4 , and 72.3 ± 7.9 . Progressive motility significantly decreased in both post-thaw groups compared to the pre-freezing stage; however, no significant difference was observed between the two post-thaw groups. The DNA integrity of the before freezing group

and the microfluidics equilibration group was close, but the level of DNA fragmentation in the conventional equilibration group significantly increased compared to the before freezing group. The normal morphology of sperm in the microfluidics equilibration group was comparable to pre-freezing results, with no statistically significant differences observed.

Conclusion: The gradual addition of CPA in the microfluidics chip reduces the damage caused by freezing on sperm viability, motility, DNA integrity, MMP, and normal morphology.

Keywords: Sperm, Cryopreservation, Microfluidics, Cryoprotectant

P-41: Effects of Exosome Therapy on Oxidative Stress and Sperm DNA Fragmentation

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Background: Oxidative stress plays a critical role in cellular dysfunction, particularly in testicular cells subjected to environmental challenges such as hyperthermia. Understanding the mechanisms underlying this process is essential for developing effective therapeutic strategies. This study evaluates the effects of hyperthermia (Hyp) on oxidative stress markers, glutathione peroxidase (GPX) activity, DNA fragmentation, and the potential protective effects of exosomes (EXO).

Materials and Methods: Male NMRI mice were kept under standard conditions. After ethical approval, anesthesia was administered, and hyperthermia (43 °C, 20 minutes, every other day for five days) was induced. Exosomes were isolated via sequential centrifugation. Oxidative stress markers (ROS, GSH/GSSG, GPX) and DNA fragmentation were analyzed.

Results: Oxidative stress markers showed significant alterations following hyperthermia. ROS levels increased in the Hyp group compared to controls, indicating elevated oxidative stress, while EXO treatment mitigated this effect. GPX enzyme activity decreased in the Hyp group, suggesting compromised antioxidative defense, whereas treatment improved GPX levels. GSSG concentrations rose in the Hyp group, signifying oxidative stress, but were significantly reduced in the EXO-treated group. Fragmentation analysis demonstrated reduced genomic damage in the EXO-treated group compared to the hyperthermia group compared to the Hyp group. DNA fragmentation analysis demonstrates improvements in cellular integrity in the treated group.

Conclusion: These findings indicate that hyperthermia increases oxidative stress, as evidenced by elevated ROS and GSSG levels and reduced GPX activity. EXO treatment mitigates oxidative damage, restoring key antioxidative markers and improving cellular integrity. Further studies are needed to explore its molecular mechanisms and therapeutic potential.

Keywords: Exosome, DNA Fragmentation, Sperm, Oxidative Stress

P-42: Effect of Rutin on Serum and Testicular Tissue Biochemical Factors in NMRI Mice Following Treatment with Methotrexate

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Background: Methotrexate, a chemotherapy agent used in cancer treatment, increases reactive oxygen species (ROS) and oxidative stress. Rutin, a flavonoid with potent antioxidant and anti-inflammatory effects, can counteract oxidative damage by neutralizing free radicals. This study examined rutin's protective role on biochemical markers in the testicular tissue and serum of NMRI male mice exposed to methotrexate.

Materials and Methods: In this study, twenty-four adult NMRI male mice (average weight: 31 ± 3 g) were randomly divided into four groups: control, methotrexate (20 mg/kg/bw), rutin (100 mg/kg/bw), and methotrexate + rutin, and they were treated for 35 days. Following dissection, the serum samples were collected to measure the serum levels of total antioxidant capacity (TAC) and malondialdehyde (MDA). Additionally, testicular tissue samples were used to measure the levels of TAC and MDA. Data were statistically analyzed using SPSS software version 26, with One-Way ANOVA and Tukey's test. The mean difference was considered significantly different at $P < 0.05$.

Results: The methotrexate group showed a significant reduction in serum and testicular tissue TAC level when compared to the control group ($P < 0.01$). Serum and testicular tissue MDA levels increased significantly in the methotrexate group compared to the control group ($P < 0.01$). However, in the methotrexate + rutin group, serum and testicular tissue TAC level showed a significant increase compared to the methotrexate group ($P < 0.05$). Furthermore, a significant decrease in the mean serum and tissue MDA level was observed in the methotrexate + rutin group when compared to the methotrexate group ($P < 0.01$).

Conclusion: Our results showed that Rutin reduces methotrexate-induced oxidative stress in NMRI male mice by improving TAC and reducing MDA levels in both serum and testicular tissue. These findings suggest that rutin may serve as a potential antioxidant agent to mitigate methotrexate-induced oxidative damage in reproductive tissue.

Keywords: Methotrexate, Rutin, Oxidative Stress, Mice

P-43: Evaluation of The Correlation between The DNA Fragmentation Index and Human Sperm Morphology

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Background: Sperm morphological abnormalities and abnormal maturation of sperm chromatin can be considered as indicators of male fertility. Therefore, the evaluation of sperm structural abnormalities and sperm DNA damage is very important in evaluating male fertility potential. However, the pathogenesis of these disorders and the relationships between them are not fully understood, as sperm morphology, including the high density of spermatid chromatin, is unique and complex. This study aimed to determine the relationship between morphological detail abnormalities and human sperm DNA integrity using the sperm chromatin dispersion method (Halo test).

Materials and Methods: In this study, by referring to the archives of tests of the infertility treatment ward of Bahar Hospi-

tal in Shahrood, the test reports of patients who were requested for semen analysis and DNA fragmentation test (DFI) were studied. 402 reports were included in the study, and the relationship between DFI values and normal morphology values, and the percentage of sperm abnormalities was statistically analyzed using Chi-square and Spearman correlation test in SPSS software.

Results: The results of our study showed that there was a significant relationship between DFI being normal or not and sperm morphology being normal or not ($P=0.012$). The relationship between DFI and sperm head abnormalities ($P<0.001$), DFI and sperm neck abnormalities ($P<0.001$), DFI and tail abnormalities was significant ($P<0.001$), but there was no significant difference between DFI values and excess residual cytoplasm in sperm ($P=0.533$).

Conclusion: The results of our study showed that, in general, the DFI level is higher than the 15% value suggested in the semen evaluation protocols among teratozoospermia patients, and sperm morphological abnormalities are related to DFI values. Sperm quality plays a vital role in fertilization and embryo development, and subsequently in the production of healthy children. However, normal sperm parameters are not all clearly related to chromatin integrity and sperm DNA fragmentation. Therefore, sperm DNA fragmentation assay should be considered as an auxiliary role in the evaluation of male fertility.

Keywords: Sperm, Semen Analysis, Morphology, DNA Fragmentation

P-44: Lipid Profile Alterations in Male Infertility: A Comparative Study of Asthenozoospermic and Normozoospermic Samples

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Background: Male infertility is an increasing global concern, with underlying causes often remaining unclear. Sphingolipids such as ceramides and sphingosine play essential roles in cellular processes including apoptosis and differentiation, which are critical for spermatogenesis and sperm function. Emerging evidence suggests that altered sphingolipid metabolism may be implicated in reproductive disorders.

Materials and Methods: A case-control study was conducted involving two groups of men ($n=3$ each), classified according to WHO criteria. Seminal plasma was analyzed for ceramides and sphingosine using High-Performance Liquid Chromatography (HPLC). Statistical analysis was performed using independent t-tests.

Results: Significantly elevated levels of all measured sphingolipids were observed in the asthenozoospermic group ($P<0.0001$). Sphingosine levels were approximately 3.8 times higher in asthenozoospermic men compared to controls. Among ceramides, C14 showed the most notable increase (≈ 5.9 -fold), followed by C18 (≈ 4.1 -fold), C20 (≈ 4.2 -fold), and C16 (≈ 3.5 -fold).

Conclusion: The marked elevation of sphingosine and ceramide species in asthenozoospermic men suggests a significant disruption in sphingolipid metabolism, potentially contributing to impaired sperm motility. These lipids may influence sperm function by altering membrane dynamics or triggering stress pathways. The findings support the potential use of ceramides

and sphingosine as biomarkers for asthenozoospermia and offer a basis for future studies targeting lipid metabolism in male infertility. Larger-scale research is needed to confirm these results and explore therapeutic implications.

Keywords: Male Infertility, Asthenozoospermia, Ceramide, Sphingosine, Sperm, HPLC, Biomarker

P-45: Exosome Therapy in Erectile Dysfunction: A Promising Regenerative Approach

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Background: Erectile dysfunction (ED) is a common male sexual disorder linked to aging, diabetes, cardiovascular conditions, and nerve injuries. Current treatments like PDE5 inhibitors are not always effective, especially in neurovascular damage cases. Exosomes, nanosized vesicles containing bioactive molecules, play a role in intercellular communication and tissue regeneration, showing promise for ED therapy.

Materials and Methods: Animal models of diabetic and nerve injury-induced ED were used. Exosomes isolated from MSCs were characterized and injected into the corpus cavernosum. Erectile function was measured by ICP/MAP ratios. Histological and molecular analyses evaluated smooth muscle content, endothelial markers, and fibrosis.

Results: Exosome treatment improved ICP/MAP ratios increased smooth muscle content, and enhanced expression of CD31 and α -SMA. Markers of apoptosis and fibrosis, such as Caspase-3 and TGF- β 1 were downregulated. Angiogenesis was stimulated, via VEGF delivery.

Conclusion: MSC-derived exosomes demonstrate promising therapeutic effects in ED models through vascular regeneration, anti-apoptotic and anti-fibrotic actions. Clinical trials are required to validate their safety and efficacy in humans.

Keywords: Exosome, Erectile Dysfunction, Mesenchymal Stem Cells, Regeneration,

Animal Biotechnology

P-46: Effects of Hyaluronan on The Cryopreservation of Rooster Sperm: Improvements in Freezing and Cooling Results

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Background: In order to reproduce chickens and preserve biodiversity, rooster sperm cryopreservation is a crucial technique. Sperm viability and function may be impacted by oxidative stress and membrane damage brought on by the chilling and freezing procedures. A glycosaminoglycan with antioxidant and membrane-stabilizing qualities, hyaluronan has the potential to enhance the results of sperm cryopreservation. The purpose of this study was to assess how hyaluronan affected

the freezing and cooling phases of rooster sperm cryopreservation, with particular attention on antioxidant enzyme activities (GPX, TAC, and SOD) and computer-assisted sperm analysis (CASA) characteristics.

Materials and Methods: Mature roosters' semen samples were taken, and they were then preserved in a cryopreservation solution with different hyaluronan concentrations (0.5 and 1.0 mg/mL). The samples underwent regulated freezing and cooling procedures. Sperm motility, velocity, and other CASA parameters were included in post-thaw analysis. GPX, TAC, and SOD levels were measured using conventional biochemical methods to evaluate antioxidant activity. To find significant differences between the therapy groups, statistical comparisons were performed.

Results: Post-thaw sperm motility, progressive motility, and velocity were all markedly enhanced by hyaluronan supplementation ($P < 0.05$). Superior outcomes were shown by the greater concentration (1.0 mg/mL), especially in improving membrane integrity. The efficiency of hyaluronan in reducing oxidative stress during cryopreservation was demonstrated by the significantly higher levels of antioxidant enzyme activity (GPX, TAC, and SOD) in the groups treated with it.

Conclusion: By improving functional sperm parameters and strengthening antioxidant defenses, hyaluronan enhances the cooling and freezing results of rooster sperm cryopreservation. A viable method for maximizing sperm preservation in chicken reproduction is its incorporation into cryopreservation procedures.

Keywords: Sperm Cryopreservation, Hyaluronan, CASA Parameters, Cooling and Freezing

P-47: Evaluation of Ziziphora clinopodioides in Sperm Cryopreservation with No Significant Effect on Post-Thaw Antioxidant and CASA Parameters

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Background: For the preservation of genetic resources and the reproduction of ram, sperm cryopreservation is essential. By reducing cryodamage, cryoprotectants and additions are frequently utilized to improve the quality of post-thaw sperm. Ziziphora clinopodioides, commonly known as Kakuti, is a medicinal plant rich in bioactive compounds such as flavonoids, phenolic acids, and polysaccharides. Its extracts have demonstrated strong antioxidant, anti-inflammatory, and antimicrobial properties. The purpose of this study was to examine how Ziziphora clinopodioides addition in cryopreservation conditions affects the antioxidant enzyme activities (GPX, TAC, and SOD) and functional sperm characteristics measured by computer-assisted sperm analysis (CASA) of ram sperm.

Materials and Methods: Four mature rams were used to obtain semen samples, which were then split into two groups: one treated with 0.5% Ziziphora clinopodioides and the other without. The two groups underwent a routine freezing-thawing procedure. Evaluations of antioxidant enzyme activity (GPX, TAC, and SOD) as well as motility, velocity, and CASA parameters were included of the post-thaw studies. To ascertain the significance of group differences, statistical analyses were conducted.

Results: There was no statistically significant increase in total motility, progressive motility, or CASA-derived velocity pa-

rameters when Ziziphora clinopodioides was added to the cryopreservation media ($P > 0.05$). Likewise, there were no discernible variations in the antioxidant enzyme activity (GPX, TAC, and SOD) between the control group and the Ziziphora clinopodioides-treated group. These findings imply that Ziziphora clinopodioides offers no appreciable protective advantages during the cryopreservation procedure.

Conclusion: The quality of post-thaw sperm and antioxidant defenses were not significantly impacted by Ziziphora clinopodioides addition in the cryopreservation medium. It is advised that future research investigate other Ziziphora clinopodioides doses or combinations with well-known cryoprotectants in order to find any possible synergistic effects.

Keywords: Sperm, Cryopreservation, Ziziphora clinopodioides, CASA

P-48: Evaluation of Methylcellulose as a Cryoprotectant in Rooster Sperm Cryopreservation

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Background: For the preservation of genetic resources and the reproduction of poultry, rooster sperm cryopreservation is essential. By reducing cryodamage, cryoprotectants and additions are frequently utilized to improve the quality of post-thaw sperm. A polysaccharide derivative called methylcellulose has been suggested as a stabilizing agent, although nothing is known about how it affects the cryopreservation of rooster sperm. The purpose of this study was to examine how methylcellulose addition in cryopreservation conditions affects the antioxidant enzyme activities (GPX, TAC, and SOD) and functional sperm characteristics measured by computer-assisted sperm analysis (CASA) of rooster sperm.

Materials and Methods: Ten mature roosters were used to obtain semen samples, which were then split into two groups: one treated with 0.5% methylcellulose and the other without. The two groups underwent a routine freezing-thawing procedure. Evaluations of antioxidant enzyme activity (GPX, TAC, and SOD) as well as motility, velocity, and CASA parameters were included of the post-thaw studies. To ascertain the significance of group differences, statistical analyses were conducted.

Results: There was no statistically significant increase in total motility, progressive motility, or CASA-derived velocity parameters when methylcellulose was added to the cryopreservation media (p value > 0.05). Likewise, there were no discernible variations in the antioxidant enzyme activity (GPX, TAC, and SOD) between the control group and the methylcellulose-treated group. These findings imply that methylcellulose offers no appreciable protective advantages during the cryopreservation procedure.

Conclusion: The quality of post-thaw sperm and antioxidant defenses were not significantly impacted by methylcellulose addition in the cryopreservation medium. It is advised that future research investigate other methylcellulose doses or combinations with well-known cryoprotectants in order to find any possible synergistic effects. Cryopreservation, Rooster, methylcellulose

Keywords: Cryopreservation, Rooster, methylcellulose

P-49: Impact of Osmotic Agents on Ram Sperm Cryo-

preservation: Mannitol, Sorbitol, and Dulcitol at Different Concentrations

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Background: Cryopreservation of ram sperm is a crucial technology in sheep breeding and genetic conservation. The use of osmotic agents such as mannitol, sorbitol, and dulcitol in semen extenders can decrease cryoinjury and increase post-thaw sperm quality. However, the usefulness of these medicines at specified doses requires additional research. This study aims to assess the effects of mannitol, sorbitol, and dulcitol, on the post-thaw quality of ram sperm to establish the best suited osmotic agent.

Materials and Methods: Semen samples were taken from four adult rams, pooled to decrease variability, and divided into three experimental groups: mannitol, sorbitol, and dulcitol. The cryopreservation technique followed a conventional protocol, and post-thaw sperm quality was tested by CASA. Evaluated metrics were total motility, progressive motility, curvilinear velocity (VCL), straight-line velocity (VSL), and average path velocity (VAP). Data were examined using ANOVA, with p value < 0.05 regarded as statistically significant.

Results: Dulcitol displayed the best effectiveness in retaining post-thaw sperm motility and velocity characteristics, exceeding both mannitol and sorbitol. Mannitol demonstrated moderate results, notably in preserving velocity metrics. Sorbitol, at both doses, displayed the lowest efficiency in sustaining sperm quality, presumably due to its poor osmotic and metabolic support capabilities.

Conclusion: Dulcitol is a highly efficient osmotic agent for cryopreserving ram sperm, delivering exceptional preservation and motility outcomes. Mannitol also shows promise, but sorbitol was less successful under the testing conditions. These findings underline the necessity of accurate selection and concentration adjustment of osmotic agents in ram sperm cryopreservation methods.

Keywords: Cryopreservation, CASA, Ram Sperm

P-50: Evaluating the Impact of Hormonal Synchronization Protocols on Fertility in Indigenous Iranian Cattle: A Systematic Review and Meta-Analysis (2012–2025)

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Background: Improving reproductive performance in indigenous Iranian cattle is vital for boosting national livestock productivity. Hormonal synchronization protocols—such as Ovsynch, controlled internal drug release (CIDR), and exogenous gonadotropins—have shown potential in enhancing fertility outcomes. This systematic review evaluates the effectiveness of these interventions from 2012 to 2025, aiming to inform more

effective reproductive management strategies in native breeds.

Materials and Methods: A systematic search identified 10 clinical trials conducted between 2012 and 2025, involving 713 indigenous Iranian cattle. Evaluated protocols included Ovsynch (GnRH + PGF_{2α}), human chorionic gonadotropin (hCG), equine chorionic gonadotropin (eCG), and combinations involving CIDR inserts and vitamin E. Pregnancy rate was the primary outcome. Data were synthesized using a random-effects meta-analysis model to account for interstudy heterogeneity.

Results: Hormonal protocols significantly improved fertility, with pregnancy rates ranging from 55% to 70% in treated groups, versus 26% to 40% in controls. The CIDR + eCG combination was most effective, achieving a 70% pregnancy rate versus 40% in controls. Other treatments, including hCG alone and GnRH with vitamin E, also demonstrated significant benefits. Meta-analysis showed a pooled risk difference (RD) of 0.272 (95% CI: 0.221–0.323), with eight studies reporting statistically significant improvements (P<0.05). Two smaller trials showed positive, though non-significant, trends. Forest plots consistently favored hormonal protocols, with most confidence intervals not crossing the null line. A hierarchical ranking identified CIDR + eCG, hCG, and Ovsynch as top-performing interventions.

Conclusion: Hormonal synchronization protocols substantially enhance fertility in indigenous Iranian cattle, supporting their broader adoption in national reproductive management programs. Future large-scale, breed-specific studies are recommended to optimize protocol effectiveness across varied environmental conditions.

Keywords: Hormonal Synchronization, Fertility, Indigenous Iranian Cattle, Systematic Review

Embryology

P-51: The Effect of Resveratrol on The Expression of Autophagy-Related Genes During Ovarian Aging in Mice

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Background: Autophagy is a crucial mechanism which prevents the accumulation of toxic materials by degrading harmful intra-cellular components. Numerous investigations have shown that dysregulation of autophagy can lead to a reduction in follicular reserve and potentially cause premature ovarian aging. Resveratrol is a polyphenolic compound with anti-oxidant and anti-aging properties. The aim of this research was to investigate the effect of resveratrol on the expression of genes associated to autophagy during the aging of NMRI mice ovaries.

Materials and Methods: In this study, female NMRI mice (8 wk, 25 g) were randomly distributed to the control and treatment groups (n=10 per group). The control group was given ordinary distilled water until the end of the 6 or 12 months, whereas the treatment group received water containing 30 mg/L resveratrol for identical periods. Eventually, mice were sacrificed, and their ovaries were bilaterally harvested for gene expression analysis and histological purposes.

Results: The RT-PCR results revealed that the ATG7 and Lc3b genes were significantly downregulated ($P<0.05$) in the treatment group (6-month) compared to the corresponding control group; nevertheless, the mRNA levels of ATG5 and Becn1 remained unaffected following resveratrol therapy (6-month). Moreover, the expression levels of ATG7, Becn1, and Lc3b were significantly higher ($P<0.001$) in 12-month-old control mice than in 6-month-old control mice. However, treatment with resveratrol for up to 12 months significantly ($P<0.001$) reduced the levels of ATG7, Becn1, and Lc3b. Moreover, H&E staining indicated that resveratrol significantly ($P<0.05$) boosted the quantity of primary, secondary, and antral follicles in six-month-old mice, but atretic follicles were diminished. The administration of resveratrol for 12 months just reduced the number of atretic follicles.

Conclusion: Taken together, our findings indicated that resveratrol has the potential to decrease elevated autophagy genes and reduce atretic follicles during ovarian aging.

Keywords: Ovarian Aging, Autophagy, Resveratrol

P-52: Effect of Adding Epidermal Growth Factor on *In Vitro* Maturation of Mouse Germinal Vesical Oocytes and Subsequent Fertilization Potential

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Background: Oocyte *in vitro* maturation (IVM) is an interesting technology recognized for its safety and simplicity. It is primarily offered to women with poor oocyte maturation and individuals at risk of losing fertility for fertility preservation. This study aimed to determine the effects of epidermal growth factor (EGF) supplementation on the IVM outcomes of mouse germinal vesicle (GV) oocytes.

Materials and Methods: In this experimental study, following superovulation by using PMSG hormone, immature oocytes were collected from 8-weeks old NMRI mice and randomly distributed into the control and experimental groups. The basic culture medium was α -MEM supplemented with 10% fetal bovine serum (FBS), 50 mg/l streptomycin, 60 mg/l penicillin. The experimental group received 20 ng/ml EGF. After 24 hours incubation at 37°C, for IVF, capacitated spermatozoa were added to in vitro matured oocytes. Five hours later, the oocytes were cultured in fresh droplets of M2 medium for 24 hours and assessed for cleavage to the two-cell stage.

Results: Oocyte maturation rates were determined based on the presence or absence of the first polar body. As compared with the control group, the rate of maturation was significantly increased in the EGF ($P<0.05$) group. Moreover, the experimental group showed higher rate of two-cell development, than the control group ($P<0.05$).

Conclusion: This study indicated that adding EGF to the IVM medium improves the maturation rates of immature oocytes, which may affect the success of in vitro fertilization and early embryo development.

Keywords: In Vitro Maturation, Epidermal Growth Factor, In Vitro Fertilization

P-53: The Effect of Sellenium on DNA Integrity AND Sperm

Nuclear Maturation in NMRI Mice Following T-treatment With Cyclophosphamide

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Background: Cyclophosphamide, a widely used chemotherapy drug, despite its therapeutic benefits, induces oxidative stress and causes reproductive toxicity. This study evaluated the effect of selenium, a potent antioxidant, on sperm DNA integrity and nuclear maturation in NMRI mice following cyclophosphamide treatment.

Materials and Methods: Thirty-two adult male NMRI mice were randomly divided into four groups: control, cyclophosphamide (intraperitoneal injection, 100 mg/kg, once a week), selenium (intraperitoneal injection, 1 mg/kg, every day), and cyclophosphamide + selenium. Treatments were administered for 35 days. After dissecting the mice, the caudal region of the epididymis was isolated in Ham's F10 culture medium. Sperm were extracted and assessed for integrity of DNA double-stranded structure using acridine orange staining and for nuclear maturity using aniline blue staining. Data were analyzed using SPSS software with one-way ANOVA and Tukey's test; differences were considered statistically significant at $P<0.05$.

Results: A significant decrease in the mean sperm nuclear maturity ($P<0.05$) and integrity of DNA double-stranded structure ($P<0.001$) was observed in the cyclophosphamide group compared to the control group. These side effects were compensated for in the cyclophosphamide + selenium group compared to the cyclophosphamide group.

Conclusion: Our results showed that cyclophosphamide impairs sperm nuclear maturation and DNA integrity in NMRI mice by inducing oxidative stress. However, co-administration of selenium effectively reduced these adverse effects, highlighting its potential as a protective agent against cyclophosphamide-induced reproductive toxicity.

Keywords: Cyclophosphamide, Selenium, DNA Damage, Mice

P-54: The Effect of Simultaneous Treatment of Sitagliptin and MYO-Inositol on Sperm Parameters in Diabetic Mice

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Background: Sitagliptin is a dipeptidyl peptidase-4 inhibitor indicated for the treatment of type 2 diabetes mellitus. Despite its therapeutic benefits, it induces oxidative stress and causes reproductive toxicity. Therefore, this study investigated the potential antioxidant effects of myo-inositol on sperm parameters in diabetic mice treated with sitagliptin.

Materials and Methods: In this study, twenty-four adult NMRI male mice were randomly divided into five groups: control, diabetic (streptozotocin [150 mg/kg] + nicotinamide [110 mg/kg]), diabetic + sitagliptin (30 mg/kg/bw), diabetic + myo-inositol (300 mg/kg/bw), and diabetic + sitagliptin + myo-inositol and they were treated for a period of 35 days. After dissecting the mice, the caudal epididymis was isolated in Ham's F10 culture medium, and the extracted sperm were analyzed for various

sperm parameters. Data were statistically analyzed by spss software, One-Way ANOVA and Tukey's test, and the means difference was considered significant at the $P < 0.05$.

Results: The diabetic group showed a significant reduction in the mean number, viability, motility, morphology and membrane integrity of the sperm cells when compared to the control group ($P < 0.05$). These parameters significantly decreased in the diabetic + sitagliptin group compared to the control group ($P < 0.05$) and didn't show a significant difference compared to the diabetic group ($p > 0.05$). These side effects were compensated for in the diabetic + sitagliptin + myo-inositol group compared to the diabetic + sitagliptin group.

Conclusion: Our results revealed that sitagliptin treatment significantly impairs sperm quality in diabetic mice. Simultaneous treatment of sitagliptin and myo-inositol effectively mitigates these adverse effects.

Keywords: Sitagliptin, Myo-Inositol, Sperm Motility, Mice

P-55: Metformin Reverses Prostatitis-Related Infertility: Recovery of Sperm Quality in A Rat Model of Chronic Non-Bacterial Prostatitis

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Background: Male infertility is increasingly linked to chronic non-bacterial prostatitis (CNP), an inflammatory condition that disrupts prostate function and impairs spermatogenesis. Because safe, targeted therapies are scarce, we evaluated whether metformin, a well-characterized antidiabetic drug with anti-inflammatory and antioxidant properties, could rescue fertility potential in a CNP rat model.

Materials and Methods: Twenty-four adult Wistar rats were randomly assigned to four groups ($n = 6$ each): healthy controls, untreated CNP, CNP + cernilton (benchmark phytotherapy), and CNP + metformin. CNP was induced by a single intraprostatic injection of 1 % carrageenan. Treatment regimens (100 mg kg⁻¹ day⁻¹, oral) were administered for 21 days. Primary fertility-oriented endpoints were epididymal sperm count, progressive motility, and viability; secondary endpoints included prostatic index (PI) and serum inflammatory mediators, prostate-specific antigen (PSA), interleukin-17 (IL-17), and interferon- γ (IFN- γ). **Results:** Untreated CNP markedly reduced sperm count (-80 %), motility (-49 %), and viability (-48 %) versus healthy controls, accompanied by elevations in PI (+104 %) and inflammatory markers (all $P < 0.05$). Metformin therapy restored sperm count to 61 % of control values and normalized motility and viability to 83 % and 82 % of baseline, respectively. Concomitantly, metformin lowered PI, PSA, IL-17, and IFN- γ to near-control levels. Metformin demonstrated potent fertility-restorative effects in CNP by improving sperm parameters and downregulating pro-inflammatory markers.

Conclusion: These findings suggest a novel therapeutic role for metformin in managing prostatitis-associated male infertility. Its affordability, safety profile, and pleiotropic benefits make it a compelling candidate for future clinical trials in human male

reproductive medicine.

Keywords: Chronic Prostatitis, Metformin Repurposing, Male Reproductive Health, Cytokine Modulation, Prostatic Inflammation

P-56: The Effect of Autologous Platelet Rich Plasma (PRP) Intraovarian Injection on Transcript Levels of Mitochondrial TFAM Gene in Patients with Polycystic Ovary Syndrome

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Background: Polycystic ovary syndrome (PCOS), a common endocrine disorder affecting women of reproductive age, is associated with metabolic dysfunction. Mitochondrial dysfunction has emerged as a potential contributor to the pathogenesis of PCOS, which impact on oocyte quality. Genes encoding for mitochondrial such as transcription factor A (TFAM) is involved in mitochondrial biogenesis. Platelet-Rich Plasma (PRP), an autologous blood product, has indicated can influence mitochondrial activity. The effect of ovarian injection of autologous platelet rich plasma on transcript Levels of Mitochondrial TFAM gene in patients with PCOS.

Materials and Methods: 33 oocytes in different stages of maturation obtained from 22 PCOS patients who underwent *in vitro* fertilization (IVF)/intra-cytoplasmic sperm injection (ICSI). The patients divided to 2 groups: 1) group PRP intraovary injection, and 2) group without PRP injection. RNA transcript level of TFAM was quantified by single-cell TaqMan real-time (qRT-PCR).

Results: There was no significant difference between two groups of the relative expression TFAM gene in germinal vesicle (GV) stage oocytes ($P = 0.81$). A significant difference was observed between two groups of the relative expression level of TFAM gene at the stages of metaphase I (MI) and MII ($P = 0.001$ and $P = 0.007$).

Conclusion: PRP intraovarian injection can influence mitochondrial transcript level TFAM gene and improve oocyte quality in PCOS patients.

Keywords: Polycystic Ovary Syndrome, Platelet-Rich Plasma, Quantitative Real-Time Polymerase Chain Reaction, TFAM, Mitochondria

P-57: Nanoparticles as Cryoprotective Agents in Sperm Cryopreservation: A Systematic Review

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Background: Cryopreservation is the most important step of sperm cell storage for use in artificial insemination. During

cryopreservation, sperm may undergo functional and structural alterations from various factors responsible for reactive oxygen species (ROS) production and ice formation. To avoid sperm from any toxic effects of these factors, other components should be added to the sperm culture medium. Nanoparticles have many potential applications in reproductive biology. Due to the size and biological and chemical properties of nanoparticles, they are classified into different groups. In this study, we aimed to investigate the effects of nanoparticles on sperm during freezing process.

Materials and Methods: The search strategy was conducted in PubMed and Google Scholar. Available literature explored with “sperm”, “Freezing”, and “nanoparticle” Mesh Terms from 2020 to 2025. Review papers were excluded, and only 21 articles were original and related to our topic.

Results: Various types of nanoparticles were utilized as additives to the freezing medium to prevent issues related to freezing. Metal nanoparticles (silver, zinc, cerium, selenium, etc.), antioxidant nanoparticles, and herbal nanoparticles (curcumin, berberine, etc.) were introduced. Metal nanoparticles (silver, zinc cerium, selenium ...), antioxidant nanoparticles, and herbal nanoparticles (curcumin, berberin, ...) were introduced. Nanoparticles improved total motility, average path velocity, plasma membrane integrity, DNA integrity, morphology, apoptosis status (Annexin V-PI), and acrosome integrity. The total antioxidant capacity (TAC) and DNA fragmentation were dependent on concentrations. Moreover, nanoparticles reduced malondialdehyde (MDA), hydrogen peroxide, and nitric oxide. However, some nanoparticles had adverse effects on sperm (magnesium oxide nanoparticles) and may cause toxicity.

Conclusion: This study showed that nanoparticles were valuable additive materials that can be utilized to protect sperm quality and fertility potential. Optimal concentrations of nanoparticles can promote the efficiency of cryopreservation, making them a promising drug delivery system for the preservation of spermatozoa against cryodamage and improving the quality of cryopreserved sperm.

Keywords: Nanoparticle, Cryopreservation, Sperm, Cryoprotective Agents

P-58: Oxidative Damage in Epididymis and Blood of Mice Treated with Juvenoid Fenoxycarb

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Background: Pesticides usage has been increasing due to their application in various fields including agriculture. Nowadays, concerns regarding the effects of insecticide residues in environment, food, and also exposure to animals are on the rise. A class of insecticides called juvenoid (insect growth regulators) includes fenoxycarb (FXB), as a carbamate insecticide, mimic the action of juvenile hormones that blocks metamorphosis of insect larva to adult. Poorly understood about the impact of FXB on the mammalian reproductive system following entrance of juvenoid to the environment. There is a link between the action of pesticides and induction of oxidative stress (OS) as a key mechanism for induction of toxicity of environmental pollutants.

Materials and Methods: In current work, we could evaluate the changes in OS content of epididymis and blood in FXB-

treated mice. The groups of mice were as negative control, pseudo-control (sham), and experimentals (via IP, receiving conc. of 0.5, 1 & 2 mg/kg b.w., every other day for 14 days). The changes in amounts of OS biomarkers viz. reactive oxygen species (ROS), total antioxidant capacity (TAC), and carbonyl proteins (CP) were recorded in epididymis and blood samples.

Results: Our data showed the deleterious effect of FXB in mice proven by a mild increase in amounts of ROS and CP, and a severe decrease in TAC value in both epididymis and blood samples.

Conclusion: In conclusion, based on the clear findings in this study, it is feasible that use of FXB will affect tested mammalian reproductive system confirmed by the induction of OS damages.

Keywords: Juvenoid, Epididymis, Blood, Free Radicals, Oxidative Damage

P-59: Fenoxycarb Dilemma: Alterations in Oxidative Stress Biomarkers of Mouse Testis

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Background: Fenoxycarb, a carbamate insecticide, inhibits development in pests, and its detection in environments is concerning because of its widespread application. It regulates insect growth by mimicking the juvenile hormone (JH), preventing the insect from reaching maturity. At the molecular level, fenoxycarb considerably inhibits ATP generation and decreases glucose consumption. However, there is a lack of information on the effects of fenoxycarb on the function of testes, but it is expected to be harmless to them. Pesticides may induce oxidative stress (OS) leading to imbalance between the generation of free radicals and levels of antioxidants. The OS is a key mechanism for environmental pollutant-induced toxicity. In this study, we evaluated the alteration in the OS biomarkers of fenoxycarb-exposed mice testis.

Materials and Methods: Animals were divided into negative control, pseudo-control (sham), and experimental groups (via IP, receiving conc. of 0.5, 1 & 2 mg/kg b.w., every other day for 14 days). The changes in levels of OS biomarkers namely ROS, lipoperoxidation (LPO/MDA), and total antioxidant capacity (TAC) value were recorded in testis homogenates.

Results: Data revealed that upon fenoxycarb treatments, the ROS and MDA levels were augmented, but TAC was declined, concentration-dependently.

Conclusion: In brief, these results suggest that fenoxycarb poses high potential risk to mouse reproduction. It could induce testicular toxicity in mice as confirmed by altered OS biomarkers levels, leading to testis dysfunction.

Keywords: Pesticide, Fenoxycarb, Testis, Oxidative Stress, Antioxidants

P-60: Hydrogen Sulfide Administration Modulates Apoptosis, Inflammation and Oxidative Stress in High-Fat Diet-Induced Testicular Dysfunction in Rats

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Background: High-fat diet (HFD) consumption contributes significantly to male reproductive dysfunction through increased oxidative stress and inflammation in testicular tissue. Hydrogen sulfide (H₂S), an endogenous gasotransmitter, demonstrates potent antioxidant properties in various tissues, including liver, kidney, and heart. This study investigated whether sodium hydrosulfide (NaHS), a H₂S donor, could ameliorate HFD-induced oxidative damage in testicular tissue and serum of male rats.

Materials and Methods: Male Wistar rats (n=36) were randomly divided into six experimental groups: control, control+NaHS (3mg/kg/day), control+NaHS (5mg/kg/day), HFD, HFD+NaHS (3mg/kg/day), and HFD+NaHS (5mg/kg/day). Following 11 weeks of dietary intervention, daily intraperitoneal injections of NaHS were administered. Oxidative stress markers, including malondialdehyde (MDA), total antioxidant capacity (TAC), total oxidant status (TOS), and total thiol groups (TTG), were assessed in both serum and testicular tissue.

Results: HFD significantly increased serum MDA (P<0.0001) and TOS (P=0.017) while decreasing TAC (P<0.05) compared to control groups. Parallel oxidative alterations were observed in testicular tissue. NaHS administration at 5mg/kg significantly reduced MDA concentrations (P<0.01) in HFD-fed rats, while both doses (3 and 5 mg/kg) effectively decreased TOS and increased TAC levels (P<0.05) in both serum and testicular tissue. Interestingly, TTG remained unchanged across all experimental groups (P=0.8102). Additionally, HFD upregulated pro-inflammatory cytokines (IL-1 β , TNF- α) and pro-apoptotic Bax gene expression while downregulating anti-apoptotic Bcl-2. NaHS treatment successfully reversed these molecular changes, improved sperm parameters, and enhanced testicular histomorphometry in HFD-fed rats.

Conclusion: NaHS administration effectively mitigates HFD-induced male reproductive dysfunction by reducing oxidative stress, attenuating inflammation, inhibiting apoptosis, improving testicular histology, and enhancing sperm parameters. These findings suggest H₂S donors may offer therapeutic potential for oxidative stress-related male infertility associated with high-fat diets.

Keywords: Hydrogen Sulfide, Oxidative Stress, Diet, High-Fat, Male Infertility

P-61: The Effect of Supplementing Freezing Media with Stevia Extract on Sperm Parameters and *In Vitro*-Fertilization Success after Freezing in Mice

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Background: Previous investigation showed that the sperm cryopreservation is associated with the release of reactive oxygen species ROS. Though a small quantity of (ROS) is essential for some of spermatozoa physiological functions, it is important to note that high levels of these molecules cause sperm damage. Therefore, governing ROS levels via the supplementation of antioxidants appears to be working. This study aimed to investigate the impact of adding Stevia hydroalcoholic extract,

an herbal antioxidant, to the freezing medium on a number of sperm parameters and following *in vitro* fertilization (IVF) success in mice.

Materials and Methods: In this study, sperms were collected from the cauda epididymis of 12 male NMRI mice and distributed into four groups (n=3 per group): the control group (untreated frozen-thawed sperm), and three experimental groups in which samples were frozen using freezing media supplemented with hydroalcoholic extract of stevia (0.1, 0.5, and 1mM). Each group was incubated for 30 minutes at 37 °C, followed by exposure to freezing conditions. After thawing, the sperm parameters and the percentage of IVF success were assessed.

Results: Our data showed that the administration of stevia in freezing media at concentrations of 0.5 and 1 mM significantly (P<0.05) increased both the quantity of sperm exhibiting normal morphology and motility. Moreover, the IVF success rate in the sperm exposed to 0.5 and 1-mM stevia was significantly (P<0.05) promoted as compared to the control group.

Conclusion: Our findings revealed that supplementing freezing media with stevia extract could promote sperm parameters and IVF success following freezing.

Keywords: Sperm Cryopreservation, Stevia, *In Vitro* Fertilization

P-62: Beneficial Roles of Pistacia Atlantica Fruit Extract on Oxidative Status and Reproductive Parameters in Male Rats

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Background: During the last decades, there have been numerous reports about the increasing rate of infertility in various populations. Pistacia Atlantica is believed traditionally to have several therapeutic properties such as fertility-enhancing properties. Objective: The current study aimed to evaluate the effects of Pistacia atlantica fruit extract on reproductive parameters in adult male Wistar rats.

Materials and Methods: In this experimental study, 40 healthy adult male Wistar rats (8 weeks, 220- 240 g) were randomly divided into control groups and given Pistacia atlantica fruit extract by gavage for 70 days at doses of 100, 200 and 400 mg/kg (n=10 per group). Testicular peroxidation levels and serum hormone levels were evaluated in each experimental group.

Results: In male rats treated with 400 mg/kg significant increases were seen in testicular (P=0.001) and epididymal (P=0.001) weights. Higher testosterone serum levels were observed in the rats received 200 (P=0.01) and 400 mg/kg (P=0.001) Pistacia atlantica fruit extract. Malondialdehyde levels were also significantly reduced (P=0.001), and the activities of superoxide dismutase (P=0.001) and glutathione peroxidase (P=0.001) in testicular tissue were increased.

Conclusion: These results indicate that Pistacia atlantica fruit extract may help improve the reproductive performance of male rats with its antioxidant and androgenic properties.

Keywords: Pistacia Atlantica, Reproductive health, Oxidative stress, Spermatogenesis

P-63: The Role of Oviductal Extracellular Vesicles in Sperm Capacitation: A Review

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Background: Capacitation is a critical maturation process that sperm undergo within the female reproductive tract, enabling them to acquire fertilizing competence. Recent studies have highlighted the pivotal role of oviductal extracellular vesicles (oEVs)—nanosized, membrane-bound particles secreted by epithelial cells—in regulating this process. oEVs deliver functional cargos such as proteins, lipids, and RNAs to sperm through membrane fusion, thereby modulating intracellular signaling pathways, calcium dynamics, and membrane remodeling events essential for capacitation.

Materials and Methods: We conducted a systematic search of [main databases: PubMed, Scopus, Web of Science] for articles published between [2010–2025]. Studies were included based on their relevance to the role of oviductal extracellular vesicles (oEVs) in sperm capacitation. The selected papers were critically analyzed for methodological quality, biological relevance, and applicability to human reproductive models.

Results: In mice, oEVs deliver the calcium pump PMCA4 to sperm via integrin- and tetraspanin-mediated fusion, rescuing fertility in PMCA4-deficient models. In cattle, region-specific oEVs from the isthmus and ampulla activate capacitation markers and preserve sperm function post-thaw. Similar effects are observed in cats and pigs, where oEVs extend sperm longevity and modulate the timing of capacitation. Preliminary human data suggest conserved roles, with oEV-like particles from Fallopian fluid influencing sperm physiology and embryo development.

Conclusion: oEVs coordinate a dual role—priming sperm for capacitation while stabilizing the acrosomal membrane until ovulation. This is achieved through the delivery of balanced cargos that modulate calcium handling, kinase cascades, and membrane composition. Incorporating oEVs or their biomimetic analogs into assisted reproductive technologies (ART) has shown promising outcomes in improving sperm quality, fertilization rates, and embryo viability. This review consolidates evidence on oEV-mediated regulation of capacitation and highlights its translational potential in Assisted Reproduction Techniques. Future directions include molecular profiling of oEV cargos, cycle-dependent functional assays, and clinical application of oEV-based supplements to enhance fertility outcomes.

Keywords: Sperm Capacitation, Oviductal Extracellular Vesicles, Acrosomal Reaction, Sperm Hyperactivation

P-44: Follicular Fluid Promotes VSELs Maintenance in Chemotherapy-Induced Premature Ovarian Failure

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Background: One of the most important issues in patients

with chemotherapy-induced premature ovarian failure (POF) is to consider new strategies for restoring fertility. It has been approved that there are different types of stem cells, like very small embryonic-like stem cells (VSELs) within ovaries, which can regenerate folliculogenesis in adults. This study aimed to confirm the maintain of VSELs in the POF patients (by CD45- & CD133+ surface markers) who have lost all ovarian follicles and mature oocytes following onco-treatments in the presence of follicular fluid (FF).

Materials and Methods: Vitrified-warmed human ovarian cortical strips of transe sexual and chemo-POF patients were cultured on agar for one week in four groups based on the using the FF: (I) BMT group; transe sexual patients (T) ovarian tissue in base medium (BM), (II) FFT group; transe sexual patients ovarian tissue in FF, (III) BMP group; POF ovarian tissue (P) in BM, and (IV) FFP group; POF ovarian tissue in FF. The medium was exchanged once every two days. Afterward, to confirm the presence of VSELs, cortical strips were assessed using flow cytometry for CD45- and CD133+ markers at the end of culture.

Results: The results of flow cytometry showed that there were significant increases in the number of CD45- and CD133+ cells in the FFP group (87%) compared to the BMT group (34%).

Conclusion: Based on our results, it has been concluded that FF acts as an inducer during in vitro ovarian culture and can lead to the maintaining of VSELs in the ovaries. This is very important for neo-oogenesis and primordial follicle assembly under in vitro conditions, and raises great hopes for restoring fertility in POF patients.

Keywords: Human Ovarian Culture, VSELs, Follicular Fluid, Chemotherapy, Premature Ovarian Failure

P-65: Metformin-Loaded Exosome Improved Ovarian Function in The Rat Model of Premature Ovarian Failure

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Background: Premature ovarian failure (POF) is a serious ovarian dysfunction characterized by amenorrhea, elevated gonadotropin levels, reduced estradiol levels, and ovarian atrophy occurring in women under the age of 40. This condition often leads to infertility and presents a significant clinical challenge. Recent studies have highlighted the regenerative potential of exosomes (Exos) in restoring ovarian function in POF. In the present study, we investigated the therapeutic effects of Exos loaded with metformin in a rat model of POF.

Materials and Methods: Exos were isolated from serum samples using ultracentrifugation and characterized by dynamic light scattering (DLS), transmission electron microscopy (TEM), scanning electron microscopy (SEM), and western

blotting. Metformin was loaded into Exos via the sonication method. Forty-six female rats were randomly divided into five groups: control, POF, metformin, Exos, and Exos-loaded metformin. POF was induced by intraperitoneal injection of cyclophosphamide (CTX) daily for 14 consecutive days. Eight weeks after treatment, ovarian morphology and follicle counts were assessed using hematoxylin-eosin and Masson's trichrome staining.

Results: Histopathological evaluation revealed a significant increase in the number of atretic follicles and a decrease in normal follicles in the POF group compared to controls ($P<0.05$). Following treatment, the number of morphologically normal follicles increased, while atretic follicle numbers declined, particularly in the Exos-loaded metformin group ($P<0.05$). Masson's trichrome staining demonstrated that treatment with metformin-loaded Exos effectively reduced collagen fiber deposition, indicating amelioration of ovarian fibrosis.

Conclusion: Overall, our findings suggest that exosome-based delivery of metformin represents a promising therapeutic strategy for modulating pathological changes and restoring ovarian function in POF.

Keywords: Infertility, Premature Ovarian Failure, Exosome, Metformin

P-66: The Effect of Exosome Derived from Mesenchymal Stem Cells on The Development or Maturation of Immature Human Oocytes and The Expression of Development BMP15, GDF9 genes

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Background: In vitro maturation (IVM) technology facilitates the usage of immature oocytes, which is clinically important for the aged women. However, the maturation rate is low for the oocytes from the aged women. Adipose tissue-derived MSCs (AD-MSCs), as important mediators of intercellular communication, have been widely used to restore ovarian function and improve female fertility.

Materials and Methods: In this study, we isolated AD-MSCs-derived exosome (AD-Exo) and collected the human immature germinal vesicle oocytes, and we added these HUCMSCs-exosomes to the conventional IVM culture system. We obtained AD-Exo through mixed-method ultracentrifugation and size-exclusion chromatography. Transmission electron microscopy revealed an increase in the expression of exosome markers in the first four of thirteen fractions.

Results: Transmission electron microscopy revealed an increase in the expression of exosome markers in the first four of thirteen fractions. The highest maturation rate of oocytes treated with AD-Exo was observed. Moreover, increased expression of Gdf9 and Bmp15 was observed. The developmental rate was the highest upon treatment, which increased the total cell number in blastocysts. Embryonic development to the 2-cell stage was similar between the control and AD-Exo groups; however, development to the 4-cell stage and blastocyst was significantly increased in the AD-Exo group compared with that in the control group ($P<0.05$).

Conclusion: Based on the results, we propose that AD-Exo may provide a novel and cell free strategy in the improvement of the IVM in elderly infertile women in the future.

Keywords: Oocyte, Exosomes, Adipose Tissue-Derived MSCs, In Vitro Maturation

P-67: Investigating The Effects of Polyethylene Terephthalate (PET) Nanoplastics and Lycopene (LYCO) on Rat Fertility

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Background: The widespread use of polyethylene terephthalate (PET) in food and beverage packaging raises concerns about its potential health effects, especially when PET-derived nanoplastics (PET-NPs) are released into the environment. Research has shown that lycopene (LYCO) improves fertility due to its antioxidant properties. Accordingly, this study aimed to investigate the effects of PET-NPs and LYCO on reproductive toxicity in rats

Materials and Methods: After determining the proper dose of PET-NPs (2500 mg/kg), the animals were randomly divided into 6 groups (8 rats in each group). They orally received distilled water (as a vehicle of PET-NPs), 2500 mg/kg PET-NPs, and 2500 mg/kg PET-NPs plus 5, 10, 15, and 20 mg/kg LYCO, respectively, once a day for 60 days. Animals' weights, clinical signs of toxicity (abnormal behavior and bleeding), and mortality of them were recorded weekly. In addition, biochemical, spermatogenic, histomorphometric, hormonal, and histopathological parameters were examined.

Results: 2500 mg/kg PET-NP orally resulted in high mortality with induction of internal bleeding, including nosebleeds, swollen abdomen, weakness, and fatigue. It also increased body and testicular weight, sperm morphology abnormalities (broad-headed, amorphous and separated sperm, bent neck, broken, twisted, and separated tail), and ROS levels in testicular tissue ($P<0.001$); however, it reduced sperm quality and quantity parameters (e.g., number, motility, progression, sperm viability), the nuclear volume of Leydig cells, the number of Leydig and Sertoli cells, and testosterone concentration. In addition, PET-NPs-induced DNA strand breaks were observed ($P<0.001$). Furthermore, 2500 mg/kg PET-NPs with 15 and 20 mg/kg LYCO reversed all the adverse effects of PET-NPs on testicular tissue.

Conclusion: LYCO exhibited protective effects against subchronic PET-NPs-caused male rat reproductive disorders.

Keywords: Nanoplastics, Polyethylene Terephthalate, Lycopene, Fertility, Rat

P-68: Effects of Resveratrol on Gene and MicroRNA Expression Regulating Steroidogenesis, Inflammation, and Oxidative Stress in Granulosa Cells of Normal and Polycystic Ovaries

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Background: Resveratrol, a natural polyphenolic compound found in grapes, red wine, and berries, has garnered significant attention for its diverse biological activities. Extensive research has highlighted its potential in various health domains, including cardiology, neurology, endocrinology, and reproductive health. In the context of female reproductive health, resveratrol has been shown to modulate ovarian function and steroidogenesis, primarily through the activation of sirtuins, especially SIRT1. Its role in enhancing mitochondrial biogenesis and improving reproductive outcomes has been observed in women with polycystic ovary syndrome (PCOS) undergoing assisted reproduction. However, the role of related microRNA in this pathway is not clear. The present study aims to identify the signaling pathways associated with the effects of resveratrol on microRNA in ovarian health.

Materials and Methods: Human granulosa cells (GCs) were collected from the ovaries of 50 healthy individuals (referred due to male factor infertility) and 50 women with PCOS through oocyte retrieval. After purification and identification steps (flow cytometry), cells from each individual with healthy or polycystic ovaries were divided into two parts and were cultured under treatment with a culture medium (as control) and a dose of 10 μ M Resveratrol (as treatment) for 48 hours. Gene and microRNA analysis related to various cellular pathways was performed using qRT-PCR.

Results: In PCOS, elevated miR-21-5p suppresses TGFBR2, contributing to insulin resistance and inflammation, while resveratrol reduces miR-21-5p, modulating TGFBR2 expression. High miR-9-5p levels downregulate CYP19A1, decreasing estrogen production, but resveratrol alleviates miR-9-5p expression, restoring CYP19A1. MiR-34a-5p downregulates Nrf2, SIRT1, and SIRT3, exacerbating PCOS progression, whereas resveratrol reduces miR-34a-5p, enhancing these regulators.

Conclusion: Resveratrol may emerge as a potential therapeutic agent for PCOS, offering a natural alternative to current treatments. Additionally, our research could deepen our understanding of the molecular mechanisms underlying PCOS, potentially leading to the identification of novel biomarkers for early diagnosis and targeted therapy.

Keywords: Granulosa Cells, Polycystic Ovary, Resveratrol, Inflammation, miRNA

P-69: Iron-Honey Nanocomposite Mitigates Oxidative Stress and Enhances Oocyte Quality in *In Vitro* Maturation

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Background: *In vitro* maturation (IVM) is an assisted reproductive technology in which immature oocytes are retrieved from the ovaries and matured outside the body. A major limitation in IVM is the accumulation of reactive oxygen species (ROS), which adversely affect oocyte development and quality. This study aimed to investigate the effect of an iron-honey nanocomposite (IHN), known for its antioxidant properties, on oxidative stress and oocyte quality during IVM.

Materials and Methods: Germinal vesicle (GV) oocytes were collected from 6- to 8-week-old NMRI mice and randomly assigned to control and experimental groups. The control group was cultured in standard IVM medium containing α -MEM, FSH, hCG, and FBS, while the experimental group received the same medium supplemented with IHN. After 16 to 18 hours of incubation, oocyte maturation was evaluated. Intracellular ROS levels, particularly hydrogen peroxide (H_2O_2), were measured using 2', 7'-dichlorofluorescein diacetate (DCFH-DA) fluorescent staining. The fluorescence intensity of DCF, resulting from the oxidation of DCFH, was quantified to assess ROS levels. The data were analyzed using an unpaired t-test in GraphPad Prism software with a significance threshold of $P \leq 0.05$.

Results: The results demonstrated a statistically significant decrease in ROS levels in the group treated with the IHN compared to the control. This reduction in oxidative stress was associated with improved oocyte quality.

Conclusion: The findings suggest that iron-honey nanocomposite supplementation during IVM can enhance oocyte maturation by mitigating oxidative damage.

Keywords: Oocyte, *In vitro* maturation, Iron-Honey Nanocomposite, Mouse, ROS

P-70: Effect of the Human Embryo Re-Vitrification on Embryonic Developmental Potential

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Background: Embryo vitrification is a widely used and well-established assisted reproductive technology (ART) method. In certain cases, re-vitrification may be required based on clinical judgment. Repeated vitrification avoids transferring two embryos simultaneously and reducing embryo wastage. However, concerns remain regarding the potential negative impact of vitrification on embryo development. This study evaluates human preimplantation embryos' survival and developmental potential following one or two vitrification procedures.

Materials and Methods: In this experimental study, day 3 vitrified human embryos donated for research were used in two experimental groups: vitrified ($n = 62$) and re-vitrified ($n = 63$). The study was approved by the Ethics Committee of the Royan Institute (Tehran, Iran; Approval. Embryos underwent one or two vitrification using a cryotop-based method. After cryo-storage, embryos from both groups were warmed and cultured in Sage 1-step medium until day 5 of the experiment. The num-

ber of blastocysts were recorded and survival rate, blastocyst formation rate, and the percentage of arrested embryos, were evaluated.

Results: The survival rate in the vitrified group was comparable to that of the re-vitrified group (100%). However, the re-vitrified embryos showed a significantly lower blastocyst formation rate than the vitrified group (55% vs. 70%, $P=0.02$). Additionally, the number of arrested embryos was significantly higher in the re-vitrified group (44% vs. 29%, $P=0.03$). No significant differences were observed in the distribution of blastocyst quality between the groups: good quality (27% vs. 19%), fair quality (3% vs. 3%), and poor quality (1% vs. 3%) in vitrified versus re-vitrified embryos, respectively.

Conclusion: Our results showed that in vitro development was reduced in re-vitrified embryos compared to vitrified embryos, which may indicate a potentially adverse effect of re-vitrification.

Keywords: Embryo, Vitrified, Re-Vitrified, Development

P-71: The Impact of Conventional Sperm Processing Techniques on Chromosomal Integrity and Separation of X and Y Chromosome-Bearing Sperm in Holstein Cows

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Background: In recent decades, there has been extensive discussion about using cows with superior reproductive potential to reduce mating failure and increase pregnancy per mating. This includes using genetically modified animals, selecting bulls with the ability to produce disease-resistant heifers, and those with lower incidences of retained placenta, dystocia, and postpartum infections. Additionally, more attention has been given to the use of sex-determined sperm (sperm containing an X chromosome or a Y chromosome) and X- or Y-determined embryos. This study aimed to evaluate the effect of conventional sperm processing methods (Swim-up and density gradient centrifugation; DGC) on the biological parameters (total count, motility rate, progressive and non-progressive motility, morphological characteristics), DNA fragmentation, chromatin integrity, and the expression of *SRY* and *TBLIX* genes in processed spermatozoa.

Materials and Methods: Approximately 25 semen samples from Holstein cattle were transferred to the laboratory for 20 minutes at 25°C in the dark. After macroscopic evaluation, semen was divided into three groups, including the control, DGC, and Swim-up groups. In the Swim-up group, semen was mixed with Ham's F10 and incubated at 37°C for 40 minutes. Semen in the control group was washed with Ham's F10 and centrifuged at 700xg for 7 minutes. In the DGC method, semen was mixed with 80% and 40% SpermGrad and centrifuged at 500xg for 5 minutes. The biological parameters of spermatozoa (to-

tal count, total motility rate, progressive and non-progressive motility rate, and normal morphology) were evaluated using a Computer-Assisted Semen Analyzer (CASA). The expression of *SRY* (spermatozoa containing X chromosome) and *TBLIX* genes (spermatozoa containing Y chromosome) was detected using RT-PCR. DNA Fragmentation and chromatin integrity of spermatozoa in each group were investigated using Papanicolaou and Aniline Blue staining.

Results: The highest and lowest total motility rates of spermatozoa were detected in the Swim-up and control groups ($74.51 \pm 5.6\%$ vs. $50.76 \pm 4.9\%$, respectively) ($P \leq 0.05$). The most progressive motility of spermatozoa was demonstrated in the Swim-up preparation method ($57.96 \pm 5.8\%$), compared to the control group ($38.34 \pm 2.7\%$) ($P \leq 0.05$). Both the DGC and Swim-up processing methods improved the number of spermatozoa with normal chromosomal structure and chromatin integrity. In the control group, sperm chromatin integrity was only $28 \pm 1.22\%$, which was significantly lower than in the other groups ($P \leq 0.05$). The most and least DNA fragmentation and chromatin integrity were demonstrated in the control and Swim-up methods, respectively ($P \leq 0.05$). RT-PCR indicated that sperm processing methods significantly influence the separation of sperm containing X and Y chromosomes. The DGC and Swim-up methods yielded the highest percentages of sperm containing X and Y chromosomes, respectively ($P \leq 0.05$). The expressions of the *SRY* gene in processed sperm were 53.52%, 76.58%, and 27.96% in the control, Swim-up, and DGC preparation groups, respectively ($P \leq 0.05$). Conversely, the expression of the *TBLIX* gene in the control, DGC, and Swim-up groups were 46.49%, 21.74%, and 72.03%, respectively ($P \leq 0.05$).

Conclusion: Swim-up and DGC processing methods impacted the expression of genes associated with sex chromosomes, indicating their potential role in sex-selection strategies during assisted reproductive procedures.

Keywords: Sperm Containing X and Y Chromosomes, Sperm Preparation Technique, Swim-up Method, DGC Technique

P-72: Artificial Intelligence in Embryo Selection for IVF: A Systematic Review of Accuracy, Live Birth Rates, and Ethical Implications

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Background: Embryo selection remains a critical determinant of IVF success. While traditional morphology-based grading suffers from subjectivity, artificial intelligence (AI) algorithms promise improved objectivity and predictive power. This systematic review synthesizes evidence on AI's accuracy in selecting viable embryos, its impact on live birth rates (LBR), and associated ethical challenges.

Materials and Methods: A PRISMA-compliant search was conducted in PubMed/MEDLINE, Embase, IEEE Xplore, and Cochrane Library (2020-2025). Included studies compared AI (e.g., deep learning, time-lapse imaging algorithms) to conventional embryo selection in IVF. Primary outcomes were embryo selection accuracy (AUC, sensitivity/specificity) and LBR; secondary outcomes included ethical concerns (e.g., data bias,

transparency). Risk of bias was assessed using QUADAS-2 for diagnostic studies and ROB-2 for RCTs. Random-effects meta-analyses were performed where applicable.

Results: From 1,250 screened records, 42 studies (n=15, 689 embryos) met inclusion criteria: Accuracy: AI models achieved superior predictive performance (AUC 0.92, 95% CI 0.88–0.95) vs. embryologist grading (AUC 0.78, 95% CI 0.72–0.84; * $p < 0.001$). Live Birth Rates: Pooled data from 8 RCTs showed a 15% relative increase in LBR with AI (RR 1.15, 95% CI 1.06–1.25; $I^2 = 32\%$). Ethics: Only 12% of studies addressed bias (e.g., dataset diversity), and none validated algorithms across diverse populations.

Conclusion: AI significantly improves embryo selection accuracy and LBR but raises unresolved ethical issues regarding generalizability and clinical implementation. Standardized validation protocols and multidisciplinary guidelines are urgently needed to bridge the gap between innovation and equitable practice.

Keywords: Artificial Intelligence, IVF, Embryo Selection, Live Birth Rate

P-73: The Correlation between The amount of Follicular Fluid Exosomes with Fertilization Outcomes and Oxidative Stress Factors in Patients with Polycystic Ovary Syndrome

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Background: Polycystic ovary syndrome (PCOS) is a common reproductive disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. The quality of oocytes in PCOS patients remains poor, leading to poor pregnancy outcomes. The aim of this study was to investigate the relationship between the follicular fluid exosomes with oocyte quality and oxidative stress factors of granulosa cells in patients with polycystic ovary syndrome.

Materials and Methods: First, granulosa cells and follicular fluid were collected from ovarian follicles of healthy women and patients with PCOS who candidate for ART referred to Roya Infertility Center in Qom, Iran. Follicular fluid exosomes were measured using two methods: flow cytometry to examine exosomal surface markers, DLS to measure particle size, and Bradford test to measure exosomal concentration. antioxidant enzyme (MDA, SOD, CAT, and TAC in granulosa cells were tested. ART results such as (number of oocyte received, high-quality embryo, and pregnancy outcomes) were compared between two groups.

Results: In this study, a significant correlation was observed between the amount of follicular fluid exosomes and the amount of levels of MDA, SOD, CAT, and TAC in healthy women compared to the PCOS group ($P < 0.05$). There was also a significant correlation between the amount of follicular fluid exosomes, number of mature (MII) oocytes, fertilization, cleavage, and high-quality embryos ($P < 0.05$).

Conclusion: Our results suggest that increased levels of exosomes in follicular fluid may affect embryo development in PCOS patients, and the mechanism is partially related to antioxidant enzyme change in granulosa cells.

Keywords: Exosome, Polycystic Ovary Syndrome, Antioxidant

Enzyme, Embryo

P-74: Engineering of Chitosan Hydrogel Covered with Testicular Cell's Extracellular Matrix as An Excellent Substrate for Spermatogonial Stem Cells Adhesion and Proliferation

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Background: Successful *in vitro* transplantation of spermatogonial stem cells (SSCs) requires efficient culture systems. To mimic the natural environment, this study used a temperature-sensitive chitosan-based hydrogel scaffold coated with testicular cell-derived extracellular matrix. This scaffold supported the co-culture of testicular and spermatogonial cells, promoting SSC proliferation and differentiation into sperm-producing cells.

Materials and Methods: In this study, a chitosan-based thermos-responsive hydrogel was designed and its morphology and gelation time were investigated. Testicular cells from NMRI mice were cultured on the hydrogel for 14 days to deposit extracellular matrix, after which the scaffolds and various tests of morphology were decellularized. The effect of ECM-coated hydrogel (D-Hydrogel) on spermatogonial stem cell reproductive gene expression was evaluated using RT-PCR and compared with Hydrogel and control groups.

Results: DAPI staining confirmed the absence of cells and debris in the extracellular matrix (ECM). Coating the hydrogel with ECM increased water absorption and degradation ($P < 0.001$). DNA analysis showed significantly higher genetic content in the TC-Hydrogel group compared to Hydrogel and D-Hydrogel groups ($P < 0.001$). SSC survival was significantly higher on ECM-coated hydrogel (D-Hydrogel) than on uncoated hydrogel ($P < 0.001$). Cells on D-Hydrogel showed enhanced adhesion and elongation. Molecular analysis revealed a significant increase in SSC proliferation gene expression in the D-Hydrogel group compared to Hydrogel and control at days 7 ($P \leq 0.05$) and 14 ($P < 0.001$).

Conclusion: This study introduces thermo-sensitive hydrogel scaffolds coated with extracellular matrix of testicular cells as a suitable system for culturing and proliferating spermatogonia stem cells and possibly a suitable method for sperm production *in vitro*. However, further studies are needed to determine the effect of D-Hydrogel on differentiation of spermatogonia cells to produce sperm in the future studies.

Keywords: Hydrogel Systems, Cell Scaffold, Testicular Cells, Extracellular Matrix, Spermatogonia Stem Cells

P-75: Investigating The Stereological and Oxidative Stress Effects of Hydroalcoholic Extracts of Cynara scolymus L and Pioglitazone on Diabetic Rat Ovary

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Background: Women with diabetes frequently experience ovarian dysfunction, indicating that hyperglycemia negatively

affects reproductive health. This study aimed to assess the therapeutic effects of a combined treatment using *Cynara scolymus* extract and Pioglitazone on ovarian structure and function in a diabetic rat model.

Materials and Methods: A total of 35 female rats were randomly assigned to five groups: (1) Control (saline), (2) DM (diabetic control), (3) DM+Piog (30 mg/kg Pioglitazone), (4) DM+Cynara (400 mg/kg *Cynara scolymus* extract), and (5) DM+Piog+Cynara (combined treatment). All treatments were administered orally for 30 consecutive days. At the end of the experiment, ovarian tissues were collected for histopathological and stereological evaluations. Additionally, oxidative stress markers and apoptosis-related gene expressions (Bcl-2 and Caspase-9) were assessed.

Results: The combined treatment group (DM+Piog+Cynara) showed a significant increase in the number of preantral, antral, and Graafian follicles as well as corpus luteum volume. There was a marked decrease in atretic follicles and fasting blood glucose levels compared to the diabetic group. Moreover, malondialdehyde (MDA) levels were reduced, and antioxidant enzyme activity improved. Expression of the anti-apoptotic gene Bcl-2 increased, while Caspase-9 activity decreased in the combined treatment group.

Conclusion: The combination of *Cynara scolymus* extract and Pioglitazone effectively mitigated diabetes-induced ovarian dysfunction by reducing oxidative stress, regulating apoptotic signaling, and promoting follicular development. This combination therapy may serve as a promising complementary approach to improve reproductive health in diabetic conditions.

Keywords: Diabetes, *Cynara Scolymus* Extract, Pioglitazone, Folliculogenesis, Oxidative Stress

P-76: Effect of The Slow-Releasing H₂S Donor, GYY4137, on Oocyte Meiosis Progression: Insights for A Biphasic In Vitro Maturation System

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Background: Hydrogen sulfide (H₂S) has emerged as a critical gaseous signaling molecule in meiotic maturation, aging, and oocyte development. GYY4137, a slow-releasing H₂S donor, provides sustained H₂S delivery, unlike fast-releasing donors that induce transient concentration spikes. This study proposed that GYY4137 could promote meiotic progression by supporting coordinated nuclear and cytoplasmic maturation in oocytes and enhance the efficiency of biphasic in vitro maturation (IVM) systems.

Materials and Methods: Immature ovine cumulus-oocyte complexes (COCs) were cultured with concentrations of GYY4137 (0–500 μM) for 24 hours to determine the optimal doses based on GV rates. Concentrations of 300 μM and 500 μM were selected for further evaluation, alone and combined with 100 nM C-type natriuretic peptide (CNP), a known meiotic arrest modulator. GV rate was then assessed at 6 and 24 hours.

Results: Results indicated increasing concentrations of GYY4137 (0–500 μM) did not statistically significant differences in GV rates at 24 hours ($P > 0.05$). Based on these findings,

300 μM and 500 μM GYY4137 were selected for subsequent experiments. At 6 hours, 100 nM CNP alone and combined with GYY4137 (300 or 500 μM) significantly increased GV rates compared to GYY4137 alone ($P < 0.05$), although significantly different from controls. At 24 hours, CNP alone markedly increased GV rates compared to all other groups ($P < 0.05$). The control, 300 μM GYY4137, and 500 μM GYY4137 with CNP showed the lowest GV rates, while 500 μM GYY4137 alone showed no significant difference.

Conclusion: In conclusion, GYY4137 alone has limited efficacy in regulating meiosis progression. However, its combination with CNP enhances meiosis progression, suggesting a synergistic effect in modulating meiosis during pre-IVM culture. These findings warrant further investigation of GYY4137 as a complementary agent to optimize oocyte maturation protocols.

Keywords: Hydrogen Sulfide, *In Vitro* Oocyte Maturation, Meiosis, Blastocyst, Sheep

P-77: Comparative Evaluation of the Effect of Green-Synthesized Selenium Nanoparticles on The Viability of Spermatogonial Stem Cells in The Presence and Absence of Ascorbic Acid

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Background: Spermatogonial stem cells (SSCs), as the primary germ cells located in the basal compartment of the testis seminiferous tubes, play a fundamental role in the continuity of spermatogenesis and the maintenance of male fertility. Preserving the viability of these cells remains a major challenge in stem cell research and male infertility treatment. Recently, metallic nanoparticles with antioxidant properties—especially selenium nanoparticles (SeNPs)—have gained attention due to their protective effects against oxidative stress.

Materials and Methods: In this study, SeNPs were synthesized via a green method using plant extract, and their effects on SSC viability were evaluated in the presence and absence of ascorbic acid. Isolated SSCs were cultured in 96-well plates and treated with various concentrations of SeNPs alone (P5, P10, P20, P40, P80) or in combination with ascorbic acid (D5, D10, D20, D40, D80) for 24 hours. The MTT assay was used to assess cell viability.

Results: The results showed that green synthesized SeNPs without ascorbic acid induced the highest cell viability compared to groups treated with SeNPs synthesized with ascorbic acid in higher concentrations of 20 μg/ml.

Conclusion: Overall, these findings suggest that green-synthesized selenium nanoparticles can enhance the viability and stability of SSCs at appropriate concentrations, and may serve as a promising approach for future clinical applications in fertility preservation.

Keywords: Selenium Nanoparticles, Green Synthesis, Ascorbic Acid, Spermatogonial Stem Cells, Viability

P-78: Study The Changes of Sertoli Cell Index and Jansen Index in Simvastatin-Treated Male Rats

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Background: Simvastatin is a lipid-lowering agent. It reduces the synthesis of cholesterol in the liver and reduces the intracellular concentration of cholesterol. Studies have shown that simvastatin causes blockage of the spermatogenesis tubules.

Materials and Methods: Thirty-six male rats were divided into 3 groups. Group 1 served as control, group 2 and 3 animals were treated with simvastatin doses of 0.5 and 1 mg/kg wt. animals were treated for 60 days. After treatment, the testis was removed and stained, and the seminiferous tubules' parameters were investigated.

Results: The thickness of the seminiferous Sertoli cell and Jansen index of seminiferous tubules at high doses of simvastatin was significantly decreased.

Conclusion: High doses of Simvastatin have a negative effect on the reproductive system

Keywords: Seminiferous Tubules, Simvastatin

P-79: Protection against Oxidative Stress in Cryopreserved Sperm Using Zinc and Copper-Doped Hydroxyapatite Combined with Glutathione and Raffinose

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Background: Among other aspects, oxidative stress plays a key role in sperm cryodamage. This investigation explored whether a medium with zinc, copper-doped hydroxyapatite, glutathione, and raffinose would enhance antioxidant status and redox enzyme function in frozen-thawed sperm in mice.

Materials and Methods: Sperm from 10 albino mice were assigned to six groups using commercial or experimental cryo-media containing hydroxyapatite, glutathione, and raffinose, individually or combined. Following 72 hours of freezing at -196°C, samples were thawed and analyzed for antioxidant and oxidant levels, lipid and protein peroxidation, and redox enzyme activities (SOD, CAT, GPX, GR).

Results: The H+GSH+R medium showed increased TAC pre-freezing ($P=0.002$), though this difference was not significant post-thaw. TOS levels were significantly lower in the H+GSH+R group at both time points ($P<0.0001$), suggesting enhanced oxidative stress protection. Additionally, lipid peroxidation (MDA content) was significantly lower in the GSH-only medium ($P=0.003$), while protein oxidation (carbonyl content) was significantly reduced in the H-alone and H+GSH+R media ($P=0.001$ and $P=0.006$, respectively). The redox enzyme activities (SOD, CAT, GR, and GPX) were also significantly higher in the H+GSH+R medium compared to the commercial control.

Conclusion: Zinc- and copper-doped hydroxyapatite with glutathione and raffinose efficiently counteract oxidative stress in addition to maintaining redox homeostasis in frozen sperm, providing a possible means to improve preservation methods.

Keywords: Oxidative Stress, Sperm Cryopreservation, Raffi-

nose, Hydroxyapatite, Glutathione

P-80: Enhancement of Sperm Motility, Viability, and DNA Integrity Using Zinc And Copper-Doped Hydroxyapatite Combined with Glutathione and Raffinose during Cryopreservation

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Background: Cryopreservation typically causes changes in sperm motility, viability, and integrity. The current experiment analyzes how a cryoprotective medium containing zinc and copper-doped hydroxyapatite, glutathione, and raffinose would affect post-thaw sperm quality in mice.

Materials and Methods: Sperm from 10 albino mice were divided into six groups and cryopreserved using either commercial or experimental media containing hydroxyapatite, glutathione, and raffinose, alone or in combination. After 72 hours at -196°C, samples were thawed and evaluated for motility, viability (eosin-nigrosine staining), and DNA fragmentation (acridine orange staining, DNA laddering).

Results: The results showed significantly higher motility in the H+GSH+R medium compared to the commercial control medium, with individual use of GSH and raffinose resulting in lower motility ($P<0.05$). DNA damage was markedly reduced in the H+GSH+R group compared to the control ($P=0.0001$), alongside a decrease in sperm mortality ($P<0.01$).

Conclusion: Copper and zinc-doped hydroxyapatite with glutathione and raffinose considerably improve sperm function and DNA integrity upon cryopreservation. It potentially presents a better alternative to conventional cryoprotectant compositions.

Keywords: Sperm Cryopreservation, DNA Integrity, Raffinose, Hydroxyapatite, Glutathione

P-81: Therapeutic Potential of Mesenchymal Stem Cell-Derived Exosomes in Infertility Management And Enhancement of IVF Outcomes A Systematic Review

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Background: Infertility caused by ovarian dysfunction, such as premature ovarian insufficiency, polycystic ovary syndrome, and gonadotoxic effects of chemotherapy, presents significant challenges in reproductive medicine. Mesenchymal stem cell-derived exosomes (MSC-Exosomes), as cell-free biotherapeutics, have gained attention due to their ability to support reproductive tissues and improve fertility outcomes.

Materials and Methods: This review examines preclinical and emerging clinical evidence regarding the effects of MSC-Exosomes on ovarian function and IVF success. The focus is on their mechanisms of action, including paracrine signaling that promotes folliculogenesis, reduces apoptosis, restores ovarian reserve, and enhances endometrial receptivity through angiogenesis, inflammation reduction, and microRNA regulation.

Results: Studies demonstrate that MSC-Exosomes can improve

oocyte quality, increase endometrial thickness, and enhance implantation and pregnancy rates. They support the natural environment of reproductive tissues, aiding in tissue repair and functional improvement.

Conclusion: Although preclinical findings are promising, further well-designed clinical trials are necessary to determine optimal dosing, delivery methods, and safety profiles. Utilizing MSC-Exosomes as a targeted, cell-free therapy could revolutionize fertility preservation and IVF outcomes, overcoming limitations associated with stem cell transplantation.

Keywords: Mesenchymal Stem Cells, Exosomes, Infertility, In Vitro Fertilization, Endometrial Receptivity

P-82: Paternal Intake of Trans Fatty Acids Disrupts Ovarian Expression of Steroid Hormone Receptor Genes in Female Offspring: A Protective Role of Vitamin E

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Background: Paternal nutrition prior to conception has emerged as a determinant of offspring reproductive health. Trans fatty acids (TFAs), commonly present in processed foods, are known to induce oxidative stress and disrupt hormonal signaling. In contrast, vitamin E, a powerful antioxidant, could counteract these effects. This study evaluated how paternal consumption of trans fatty acids, vitamin E, and their combination affects the ovarian expression of steroid hormone receptors in female rat offspring.

Materials and Methods: Forty adult male Wistar rats were randomly assigned to four groups: standard diet (C), TFA-rich diet (CTH), vitamin E-supplemented diet (E), and combined TFA and vitamin E diet (ETH). After 60 days of dietary intervention, males were mated with females that had been fed a standard diet. Ovarian tissues were collected from adult female offspring. mRNA levels of AR, ESR1, ESR2, and PGR genes were analyzed using real-time PCR and the $2^{-\Delta\Delta C_t}$ method.

Results: All four genes showed significant downregulation in the CTH group compared to the control ($P < 0.05$). Vitamin E increased gene expression levels, although not always significantly. The ETH group showed partial recovery in expression. The most notable upregulation by vitamin E was observed in ESR2 and PGR ($P < 0.01$).

Conclusion: Paternal intake of TFAs adversely affected ovarian expression of key reproductive genes in offspring, while vitamin E demonstrated a partial protective effect. These findings highlight the crucial role of paternal diet in shaping female reproductive potential.

Keywords: Trans Fatty Acids, Vitamin E, Steroid Hormone Receptors, Paternal Diet, Gene Expression

P-83: Guardians of Reproductive Health: The Protective Role of Panax Ginseng Against Ovarian and Testicular Damage in Arsenic-Exposed Mice

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Background: This study explores the protective effects of Panax ginseng against arsenic-induced reproductive toxicity in both female and male mice. Arsenic exposure disrupts reproductive health, causing histomorphometric and inflammatory changes.

Materials and Methods: This study included 28 female and male mice, divided into four groups: a control group, an arsenic group (5 mg/kg), and two ginseng treatment groups receiving low (200 mg/kg) and high (400 mg/kg) doses via gavage for five weeks. In females, blood serum and ovarian tissue samples were analyzed for inflammatory and antioxidant factor expression profiles. In males, blood serum, sperm, and testicular tissue samples were assessed for sperm DNA/chromatin integrity and expression profiles of inflammatory and antioxidant factors after treatment.

Results: Our findings showed exposure to arsenic significantly reduced the counts of primary and secondary ovarian follicles ($P = 0.01$) and increased atretic follicles ($P < 0.0001$) compared to the controls. In contrast, high-dose ginseng treatment significantly increased primary and secondary follicle counts ($P = 0.01$, $P = 0.0008$) and reduced serum TNF- α levels ($P = 0.001$) compared to arsenic exposure. Arsenic exposure also led to decline in sperm quality, including reduced count, motility, and normal morphology, along with severe testicular damage. Both ginseng treatment groups showed significant improvements in sperm parameters and testicular histopathology. Additionally, elevated levels of malondialdehyde and differences in superoxide dismutase activity were observed among the arsenic-exposed, control, and ginseng-treated mice.

Conclusion: Our findings confirm that arsenic exposure adversely affects reproductive health in both females and males, leading to lower follicle quality, diminished sperm parameters, and significant ovarian and testicular tissue damage. Ginseng seems to be a therapeutic option, effectively improving ovarian and sperm function while offering protective benefits against arsenic-induced reproductive toxicity. Notably, both low and high doses of ginseng produced similar positive effects, suggesting its potential to mitigate the harmful consequences of arsenic exposure in both sexes.

Keywords: Panax Ginseng, Arsenic, Oogenesis, Spermatogenesis

P-84: The Protective Effects of 2-Arachidonoyl Glycerol on Cobalt Chloride-Induced Sertoli Cells Hypoxia: A Probable Therapeutic Role for Endocannabinoids

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Background: Endogenous cannabinoids (eCBs) are part of a complex biological network that play a crucial role in regulating various physiological and homeostatic processes, including

the regulation of vascular function. Recent studies have suggested significant therapeutic effects of eCBs against ischemia/reperfusion (IR) injury in the cardiac and neural cells. 2-ara-chidonoyl glycerol (2-AG) is among the most well-known eCBs that contributes to spermatogenesis and controls sperm function. The capacity of eCBs to modulate the protective responses during IR damages as well as their significant roles in regulating vascular function and reproductive homeostasis has led to the hypothesis that they may show therapeutic effects against testicular hypoxic injury. This study, therefore, aimed to investigate the effect of 2-AG on cell viability in cobalt chloride (CoCl₂)-induced Sertoli cell hypoxia to gain insight into its potential protective mechanisms.

Materials and Methods: The mouse Sertoli cells (TM4) were cultured in DMEM-F12 medium. The TM4 cells were incubated with 100 µL of the medium on a 96-well cultured plate. The cells investigated in four main groups: control, CoCl₂ (125 µM), 2-AG (1 µM) and a pretreatment group, where cells were exposed to the treatment containing medium for 24 hours. In the pretreatment group, cells were incubated with 2-AG, 24 hours before CoCl₂, while the control group was incubated only with free medium. Their effects on TM4 cell viability were then investigated using MTT assay.

Results: Cell viability decreased in cells exposed to CoCl₂, while exposure to 2-AG showed opposite effects. Pretreatment with 2-AG before CoCl₂ recovered CoCl₂-induced anti-proliferative effects. Specifically, the cellular viability of control cells was 100 ± 0.07%, which significantly decreased to 59 ± 2%, in cells exposed 125 µM CoCl₂ (IC₅₀, P<0.01). However, pretreatment with 2-AG significantly increased cell viability compared with CoCl₂ group (P<0.01) and recovered it to approximately control levels (92 ± 6%).

Conclusion: 2-AG reduces the toxicity and cell death effects of hypoxia on Sertoli cells. Inhibition of Sertoli cell death by 2-AG under hypoxic conditions, suggesting a probable clinical importance and therapeutic effects of 2-AG on infertility caused by testicular impaired blood flow. However, further research is needed to elucidate this therapeutic effect and the underlying mechanisms of protection.

Keywords: Sertoli Cell, Hypoxia, 2-AG, Cell Viability, Cobalt Chloride

P-85: Development of a Gas-Foamed, Porous 3D Scaffold Composed of Testicular ECM and Gelatin

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Background: Male infertility treatment continues to be a major

challenge, with limited effective options available. The utilization of decellularized testicular extracellular matrix (tECM) as a scaffold material offers a promising approach by providing both structural support and biological cues. In this study, a tECM-enriched gelatin scaffold was developed using a gas foaming method with interconnected pores designed to promote cell growth and function.

Materials and Methods: Ram testicular tissue was decellularized, and the efficacy of cell removal was confirmed through DAPI and hematoxylin & eosin (H&E) staining, along with quantitative DNA analysis. The quality of the decellularized tECM was validated using Alcian blue, Masson's trichrome, and Orcein staining. A composite scaffold was fabricated by blending different concentrations of tECM extract with gelatin using gas foaming technique. The mechanical strength, morphological characteristics, and cytotoxicity of the resulting hybrid scaffolds were extensively evaluated.

Results: Histological examination and DNA quantification confirmed effective removal of cellular components while maintaining key tECM elements. The scaffolds featured pore sizes between 250-310 µm, with excellent interconnectivity and optimal mechanical properties. Notably, scaffolds containing 5% tECM exhibited significantly enhanced cell infiltration, high cell attachment, and minimal cytotoxicity to testicular cells compared to other groups (P<0.0001).

Conclusion: The findings suggest that tECM-based scaffolds fabricated via gas foaming can be applied as a promising platform for in vitro spermatogenesis studies and reproductive biology research, providing a supportive environment that closely mimics native tissue conditions.

Keywords: Testicular Extracellular Matrix, Gas Foaming, Decellularization, Male infertility

P-86: In Vitro Assessment of Testicular Tissue Cultured in A Medium Containing Plasma Rich in Growth Factors (PRGF) and KnockOut Serum Replacement (KSR)

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Background: Cancer therapies often result in infertility, particularly in prepubescent males. This research evaluates a novel testicular tissue culture medium supplemented with both plasma rich in growth factors (PRGF) and KnockOut serum replacement (KSR) for its potential to support in vitro spermatogenesis.

Materials and Methods: Using five-day-old male NMRI mice, we compared the outcomes of culturing testicular tissue in a medium containing 5% KSR and 5% PRGF versus a control medium with 10% KSR alone.

Results: After 42 days of culture, the group receiving 5%KSR+5%PRGF exhibited notable degeneration of the pe-

ripheral seminiferous tubules relative to the 10% KSR group. Analysis of gene expression demonstrated significantly reduced levels of spermatogenesis-related markers (Plzf, Tek1, Tnp1) and the proliferation marker Ki67, alongside increased expression of the pro-apoptotic marker Bax. Quantitative immunofluorescence results corroborated these findings, showing marked declines in spermatogonial stem cells (PLZF), spermatocytes (SYCP-3), and proliferating cells (Ki67), with the complete absence of the post-meiotic marker ACRBP in the 5%KSR+5%PRGF group. Furthermore, the fluorescence intensity for Bax was elevated, while that for Bcl-2 was significantly diminished, compared to the 10% KSR group.

Conclusion: In summary, the combination of 5% KSR and 5% PRGF failed to support complete *in vitro* spermatogenesis and instead promoted cellular degeneration and apoptosis. The reduced expression of key germ cell and proliferation markers, alongside increased apoptotic signaling, suggests that this medium disrupts the microenvironment required for germ cell development. These results suggest that the KSR and PRGF combination, in the tested ratio, is not an appropriate formulation for maintaining or promoting spermatogenic progression *in vitro*.

Keywords: *In Vitro* Spermatogenesis, PRGF, KSR, Spermatogonial Stem Cells, Organ Culture

P-87: Systematic Review of Animal Models in Reproductive Medicine: Opportunities and Challenges in Studying Human Infertility

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Background: Animal models constitute an essential component for the advancement of reproductive medicine. They provide a necessary framework to study the molecular and physiological mechanisms of human infertility. Given the complexity of the human reproductive systems and ethical restrictions on experimentation in humans, the animal models thus become useful for simulating different pathological and physiological reproductive states. These models help to understand disease etiology and play an invaluable role in developing novel therapeutic interventional strategies.

Materials and Methods: This study is systematic review. Three scientific databases, namely PubMed, Scopus and Web of Science, were used for an extensive search for placement. A total of 5194 articles have been found at the beginning. After eliminating duplicate and irrelevant studies, titles and abstracts were screened independently by two reviewers. Selected full-text articles were proof-read according to the previously spelt inclusion and exclusion criteria. In the end, all disagreements between reviewers were solved through discussion.

Results: Ovarian physiology, spermatogenesis, embryogenesis, as well as the efficacies of assisted reproductive technologies (ARTs) have been studied using a variety of animal models: rodents (mice and rats), non-human primates, and domestic species such as sheep and pigs. Each of these models has its own advantages regarding the mimicry of human reproductive biology. Inter-species variations, ethical issues, and limited translational possibilities remain critical impediments. Yet, in the face

of these obstacles, there are a number of models with relatively evident potential for pre-clinical research.

Conclusion: The strategic selection and rigorous standardization of animal models can significantly increase their relevance and reliability in human reproductive research. No model can truly reproduce human physiology, but these systems remain one of the viable ways in understanding infertility and ameliorating ART outcomes. Genetic engineering and cross-species modeling may provide potential solutions to present shortcomings in the foreseeable future.

Keywords: Animal Models, Reproductive Biology, Human Infertility, Assisted Reproductive technologies, Translational Research

P-88: Application of Beetroot-Derived Natural Dye as An Alternative to Eosin-Nigrosin for Human Sperm Morphology Assessment

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Background: Background: Natural dyes are increasingly being used in biomedical applications because of their low toxicity, biodegradability, and sustainability compared to synthetic dyes. Traditional stains, such as eosin-nigrosin, used for sperm evaluation, raise concerns about chemical toxicity. This study evaluated the efficacy of a beetroot (*Beta vulgaris*)-derived natural dye as a non-toxic alternative dye for human sperm morphology assessment.

Materials and Methods: Beetroot pigment was extracted by homogenizing fresh beetroot in 70% ethanol (1:5 w/v), followed by agitation for 24 h at 4°C. After centrifugation (3000 rpm, 15 min) and filtration (Whatman No.1), the extract was diluted to 20% (v/v) with normal saline for staining. Ten air-dried human sperm smears (from two donors; all cells were non-viable) were stained with beetroot solution for 15 min at room temperature, then rinsed with PBS (pH=7.4) without fixation. Sperm morphology was exclusively evaluated using the WHO criteria by brightfield microscopy (1000× magnification). Eosin-nigrosin-stained slides were used for comparison.

Results: The beetroot dye successfully stained the sperm head, midpiece, and tail, providing distinct visualization and color contrast adequate for morphological differentiation according to the WHO guidelines. Importantly, the dye maintained structural integrity without causing head swelling or significant artifacts. Visual clarity for morphological assessment was comparable to that of traditional eosin-nigrosin staining. The staining method exhibited good stability.

Conclusion: Beetroot extract has significant potential as a natural, safe, and sustainable histological stain for human sperm morphology analysis. This offers an appropriate method for routine laboratory assessments. Further validation may support its integration into clinical practice.

Keywords: Beetroot Dye, Sperm Morphology, Natural Stain, Eosin-Nigrosin

P-89: The Effect of Human Follicular Fluid on Indices of

Sperm and Oxidative Stress in Normospermic Men during Cryopreservation Process

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Background: Today, sperm cryopreservation is one of the most common approaches in assisted reproductive techniques (ART) that produces irreparable damage and reduces the fertility of human sperm by producing reactive oxygen species (ROS) and oxidative stress. In this regard, researchers are looking for ways to improve freezing conditions. The aim of this study was to evaluate the antioxidant effect of follicular fluid on sperm quality of normospermic men during the freezing process.

Materials and Methods: Semen samples from 30 healthy normospermic men were divided into three groups: sham (0 min), control (1 hour), and treatment (1-hour incubation with 50% follicular fluid). After two weeks of cryopreservation, samples were thawed and analyzed for sperm parameters (motility, morphology, viability), plasma membrane integrity, mitochondrial membrane potential, DNA fragmentation, and oxidative stress markers (MDA, TAC, catalase) using ELISA. Data were analyzed using SPSS with repeated measures and Paired-Samples T Test; differences were considered significant at $P \leq 0.05$.

Results: In the control group, significant declines were observed in sperm motility (total, progressive, and non-progressive), viability, plasma membrane integrity, mitochondrial membrane potential, CAT, and TAC levels compared to the sham group. Conversely, DNA fragmentation and MDA levels significantly increased. No difference was seen in normal sperm morphology. Treatment with follicular fluid significantly improved motility, viability, membrane integrity, and TAC levels, and reduced DNA fragmentation compared to both control and sham groups. However, it showed no significant effect on morphology, mitochondrial membrane potential, CAT, or MDA levels relative to the sham group.

Conclusion: The results of this study demonstrated that the use of follicular fluid as an antioxidant in the freezing medium of sperm can improve sperm parameters after the thawing process, which may be due to the increase in total antioxidant capacity and the reduction of oxidative stress.

Keywords: Sperm, Cryopreservation, Oxidative Stress, Follicular Fluid

P-90: Mechanism of Busulfan Cytotoxicity Via Sphingolipid-Pathways on Mouse Spermatogenesis

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Background: Infertility is a common problem for young couples. Spermatogenesis involves the differentiation of spermatogonial stem cells into spermatocytes and the production of haploid spermatids. Sphingolipids are a family of lipids with a common sphingomyelin skeleton that participate in physiopathological processes of cells, including cell differentiation

and apoptosis. Busulfan is a chemotherapeutic drug for the treatment of chronic myeloid leukemia. Clinical use of busulfan, by disrupting spermatogenesis, results in oligospermia or azoospermia. The aim of this study was to investigate the changes of metabolites and genes during spermatogenesis in azoospermic individuals in order to investigate the role of sphingolipid metabolism in the process of spermatogenesis in healthy and diseased mice.

Materials and Methods: In this experimental study, 24 NMRI mice were divided into three groups: (I) immature mice (2 weeks old, $n=8$) and (II) adult mice (8 weeks old, $n=8$) and adult mice treated with busulfan at a dose of 40 mg/kg. Testes of all three groups were collected and subjected to histological, molecular and metabolic analyses. Expression levels of Asah1, Asah2, Smpd1, Smpd2, Acer1, Acer2 and CerK genes were determined using RT-qPCR and compared in all three groups.

Results: Histological evaluation confirmed active spermatogenesis in mature testes and reduced spermatogenesis in busulfan-treated mice. Molecular analysis revealed a significant increase in the expression of Smpd1, Asah2, and Acer2 in busulfan-treated mice compared with the control group ($P < 0.05$), indicating an alteration in sphingolipid metabolism during testicular azoospermia.

Conclusion: Our findings highlight the critical role of sphingolipid metabolism in regulating spermatogenesis and suggest that alterations in gene expression and levels of these metabolites can cause reduced or absent spermatogenesis. These insights pave the way for further research into sphingolipid-targeted strategies to preserve male fertility and combat infertility disorders.

Keywords: Sphingolipid, Spermatogenesis, Azoospermia, Mice, Busulfan

P-91: An AI-Powered Multi-Component Decision Support System for Embryo Selection in IVF: Integrating Deep Learning, Morphokinetics, and Large Language Models

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Background: *In Vitro* Fertilization (IVF) treatment encounters several challenges when it comes to accurately selecting the most suitable embryo for transfer. This study introduces an intelligent, multi-component decision support system that uses artificial intelligence to optimize the embryo selection process and increase the chances of a successful pregnancy.

Materials and Methods: In this project, several deep learning models were used to analyze images of blastocysts and predict outcomes in IVF. The main structure of the models consists of a multi-head architecture based on deep neural networks, which is designed to simultaneously estimate the three key components of the Gardner scoring system: expansion, inner cell mass (ICM) quality, and trophoctoderm (TE) quality. Additionally, we developed a binary classification model to predict the probability of pregnancy using both image-based data and clinical information. To improve the performance of the models, we applied various techniques, including focal loss, weighted

sampling, and K-fold cross-validation. Moreover, morphokinetic parameters extracted from time-lapse imaging data were fed into a hybrid model for embryo transfer prioritization. This model combines outputs from the Gardner index estimation, pregnancy prediction, and morphokinetic analysis to generate a comprehensive scoring system for optimal embryo selection.

Results: The AUC measures for the classifiers on expansion, ICM, and TE are 0.731, 0.734, and 0.693, respectively. Also, the AUC for pregnancy estimation is 0.61. To enhance interaction between clinicians and the system, a large language model (LLM) was integrated as a virtual medical assistant, specifically trained on scientific resources related to gynecology and infertility. This module can analyze patient records, answer clinical questions, and generate summary reports.

Conclusion: The system operates as a web-based platform with cloud infrastructure. It also supports direct connections to time-lapse imaging devices and includes a management dashboard for physicians.

Keywords: Artificial Intelligence, *In Vitro* Fertilization, Deep Learning, Machine Learning, Reproduction

P-92: Effect of Follicular Fluid-Derived Extracellular Vesicles on The Quality and Morphology of Frozen-Thawed Human Ovarian Follicles

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Background: With advances in ovarian tissue cryopreservation and subsequent transplantation, many women diagnosed with cancer can preserve their fertility. However, in some hormone-sensitive cancers and autoimmune diseases, ovarian tissue transplantation may carry a risk of reintroducing tumor cells. In these patients, in-vitro follicle culture is recommended as an alternative method which can be improved by adding specific supplements. Extracellular vesicles (EVs) are released by various cell types into the extracellular space and play a crucial role in intercellular communication. In this study, the effect of human follicular fluid (hff)-derived EV supplementation in ovarian tissue culture medium is examined.

Materials and Methods: EVs were isolated from hff (n=35) and characterized by BCA assay (Bicinchoninic Acid), DLS (Dynamic Light Scattering), WB (Western Blotting), and SEM (Scanning Electron Microscopy). Then, frozen-thawed human ovarian tissues obtained from transsexual women (n=9) were cultured in four experimental groups: control (without EV), group I (100 µg/ml EV), group II (120 µg/ml EV), and group III (200 µg/ml EV). Afterward, the follicular quality, degeneration, and developmental rate were evaluated on days 1 and 7 of the culture.

Results: BCA assay confirmed the concentration of EVs, while WB verified the presence of EV-specific markers. DLS analysis determined the EV size, and zeta potential measurements indicated their negative electric charge. SEM imaging revealed

the precise size and spherical shape of the EVs. The follicular morphology did not show a significant difference on day 1, in the presence of different doses of EV compared to the control group. However, on day 7, the quality of follicles improved significantly in groups II and III. Notably, group III exhibited a higher number of secondary follicles than the control group.

Conclusion: According to this study, hff-derived EVs have a significant dose-dependent effect on in-vitro follicular development, suggesting their potential role in enhancing ovarian follicular viability and maturation.

Keywords: Extracellular Vesicle, Fertility Preservation, Human, Ovary, Tissue Culture

P-93: The Effect of Buprenorphine and Methadone Administration on Ovarian Morphometric Characteristics and Serum Antioxidant Factors in Adult Mice

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Background: Nowadays, infertility is considered one of the most important challenges in woman of the world. Studies show that opioids can cause changes in ovarian morphology in following oxidative stress. The present study aimed to investigate the effect of methadone and buprenorphine on serum antioxidant factors and morphometric characteristics of the ovary in mice.

Materials and Methods: In this study, 24 adult female mice were randomly divided into 3 groups: control group received water daily by gavage (CTL), treatment groups received methadone (MTD; 60 mg/kg) and buprenorphine (BUP; 12 mg/kg) by gavage for 30 days, respectively. The serum levels of antioxidant marker; superoxide dismutase (SOD) and total antioxidant capacity (TAC), as well as the weight and diameters of ovary were measured.

Results: A significant decrease was observed in the size of the ovarian diameters of MTD group compared to the BUP and CTL groups (P<0.001). Animals in the BUP group had a significant decrease TAC level compared to the CTL and MTD groups (P<0.05). SOD level in treatment groups were decreased compared to CTL group, but were not significant.

Conclusion: The results of this study showed that the administration of buprenorphine and methadone can increase oxidative stress in the serum of mice and also cause ovarian atrophy and folliculogenesis and consequently leads to reduced fertility.

Keywords: Ovary, Mice, Methadone, Buprenorphine

P-94: Decellularized Calf Testis for Spermatogenesis Studies

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Background: Men's infertility and lack of production of healthy and active sperm are concerns of recent years in most

countries Preparation of extracellular matrix (ECM) from decellularization of testis tissue and spermatogenesis studies is a suitable solution to solve some problems. This study aims to decellularize calf testis by different methods to reach a suitable scaffold and introduce it in spermatogenesis studies.

Materials and Methods: Calf testis was decellularized by freeze-de freeze, 1% sodium deoxycholate (SD), 0.1% sodium dodecyl sulfate (SDS), 0.1% SDS-vacuum, 1% SDS, 1% SDS-vacuum, and Triton-X100 methods. The content of DNA, collagen, and glycosaminoglycan (GAG) was tested using the kit and staining with Hematoxylin-Eosin, Masson's trichrome, Alcian blue, and Orcein methods. The morphology of the scaffolds was analyzed with a scanning electron microscope (SEM). Biocompatibility and hemocompatibility of the scaffolds were measured.

Results: Methods of 1% SDS, 1% SDS- vacuum, and 1%SD completely removed the cells. Preservation of collagen and GAG was confirmed by staining kit and methods. The use of a vacuum showed greater porosity in the SEM images. Toxicity and hemolysis were not seen in the scaffolds.

Conclusion: Testis decellularization with 1%SDS and 1%SD, in addition to cell removal, can maintain the ECM structure to a large extent without having cytotoxic and hemolysis effects.

Keywords: Decellularization, Testis, Scaffold

P-95: The Impact of Culture Conditions on Germ Cell Markers, Fragilis and SYCP3, in Human Vitrified Ovarian Tissue

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Background: Every year, many cancer survivors face the risk of infertility due to gonadotoxic treatments. Toward fertility preservation, a novel approach explores the potential of stem cells within ovarian tissue to differentiate into oocytes. This study aimed to assess germ cell dynamics during in vitro culture by evaluating FRAGILIS, a putative germ stem cell gene, and SYCP3, a key gene in meiotic progression, over seven days. Human follicular fluid (FF) and cumulus cells conditioned medium (CCCM) were used as natural additive to support culture conditions.

Materials and Methods: Ovarian tissues from transgender do-

nors were collected under informed consent in Arash hospital (Tehran, Iran) and transported to Royan Institute Human Ovarian Tissue Bank (Tehran, Iran) within one hour. After separating the cortex, it cut into 5×10 mm² strips, and vitrified for later use. Four experimental groups were designed: I) NC: no culture; II) BM: base medium (αMEM+15%FBS); III) FF: base medium+10%FF; IV) CCCM: base medium+50%CCCM. After warming, the strips were cut in to 1×2 mm² and assigned randomly to the above groups. One fragment per sample was immediately frozen at -80°C for gene expression as NC group, while others were cultured for 7 days. On day 7, all cultured samples were stored at -80°C for assessment of FRAGILIS and SYCP3 gene expression.

Results: While most differences in gene expression were not statistically significant, a notable increase in SYCP3 and FRAGILIS levels was observed in the FF and CCCM treated groups compared to non-cultured tissues. Trends suggest that in vitro ovarian culture may enhance germ cell content.

Conclusion: The findings indicate the potential of the mentioned culture systems using follicular fluid and cumulus conditioned medium to support the proliferation and early stages of germ cell development and also highlight the need for further research to explore their role in fertility preservation strategies.

Keywords: Human Ovarian Tissue Culture, Germ Cell Development, Human Ovarian Cryopreservation, Human Follicular Fluid, Human Cumulus Cells Conditioned Medium

P-96: Protective Effect of Xylitol on Testicular Apoptosis in High-Fat Diet-Induced Obese Mice via Modulation of Key Apoptotic Markers

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Background: This study aimed to evaluate the protective effects of Xylitol on high-fat diet (HFD)-induced obesity and its impact on the expression of apoptotic markers at both mRNA and protein levels in mouse testicular tissue.

Materials and Methods: Immature male mice were randomly assigned to five groups: control (normal diet), HFD-induced obese (HFD-O), Xylitol-only (Xylitol), HFD-O + Xylitol, and HFD withdrawal + Xylitol (HFDW-O + Xylitol). Expression levels of BCL-2, BAX, and p53 mRNA were measured using qRT-PCR, while immunohistochemistry was performed to assess protein levels in testicular tissue. The BCL-2/BAX ratios at both mRNA and protein levels were also calculated.

Results: Significant (P<0.05) increase in BAX and p53 mRNA and protein levels were observed in the HFD-O group compared to the control group. Treatment with Xylitol (in both HFD-O + Xylitol and HFDW-O + Xylitol groups) significantly (P<0.05) reduced the elevated levels of BAX and p53, except in BAX+ spermatocytes, which showed no significant difference compared to HFD-O group. BCL-2 expression and the BCL-2/BAX ratio remained largely unchanged among groups, except for a significant (P<0.05) decrease in BCL-2+ spermatid cells in the HFDW-O + Xylitol group compared to the control and HFD-O groups. A notable (P<0.05) reduction in the BCL-2+/BAX+ spermatogonia ratio was also found in the HFDW-O + Xylitol group compared to HFD-O group.

Conclusion: Xylitol appears to mitigate the adverse effects of HFD-induced obesity by modulating the expression of key apoptotic markers, particularly p53 and BAX, suggesting its potential role in preserving testicular function under obesity conditions.

Keywords: Xylitol, High-Fat Diet-Induced Obesity, Testicular Apoptosis, BAX/BCL-2/p53

P-97: Machine Learning Algorithms for Predicting Oocyte Quality in *In Vitro* Fertilization (IVF): A Systematic Review

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Background: With the global infertility rate reaching 17.5%, the use of assisted reproductive technologies, particularly *in vitro* fertilization (IVF), has become a leading treatment option. In this context, oocyte quality significantly impacts the success rate of the IVF process. Given the multitude of influencing factors, utilizing artificial intelligence-based technologies can offer innovative solutions for analyzing these factors and selecting high-quality oocytes. This study examines the impact of predictive machine learning algorithms on the selection of high-quality oocytes.

Materials and Methods: In this review article, a total of 90 articles were retrieved from the databases Scopus, PubMed, and ScienceDirect using the keywords IVF, oocyte, machine learning, and artificial intelligence between the years 2020 and 2025. After reviewing titles and abstracts and removing 54 articles, 36 were selected for the preparation of this study.

Results: A machine learning model can predict oocyte quality based on laboratory and clinical data from donors, oocyte quality parameters (such as diameter, microtubule formation, polar body extrusion, morphology, and viability), and reproductive outcomes in oocyte recipients. In machine learning models, CNN algorithms are used to analyze microscopic images of oocytes and classify them based on developmental potential; SVM algorithms are used to classify oocyte quality based on imaging and morphological features; and K-MC algorithms are used to cluster oocyte characteristics and identify groups with similar fertilization potential. Results show up to a 70% improvement in accuracy and classification performance.

Conclusion: The use of machine learning leads to more accurate and personalized oocyte selection, reduces patients' psychological and financial burdens, increases IVF success rates, and enhances the quality of infertility services.

Keywords: Artificial Intelligence, *In Vitro* Fertilization, Oocyte Quality, Infertility

P-98: Fabrication of Amniotic Membrane-Based Hydrogel for Tissue Engineering Applications

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Background: The amniotic membrane (AM), a component of the placenta, is a fluid-filled sac that surrounds and protects the developing fetus. Postpartum placentas provide an easily accessible source of AM, which contains numerous beneficial biological factors but is typically discarded after birth. Amniotic hydrogel is considered a promising material for tissue engineering applications due to its angiogenic and biocompatible properties. This scaffold functions as a temporary extracellular matrix, which is gradually absorbed and eventually replaced by host tissue. Amniotic membrane hydrogels can be used both in the production of injectable scaffolds for therapeutic purposes and in bulk form.

Materials and Methods: Decellularized AMs were lyophilized and subsequently ground into powder. The resulting decellularized AM powder was digested in a solution containing 0.2 mg/ml pepsin and 0.1 N HCl for 48 hours at room temperature, using a ratio of 20 mg AM matrix per 1 ml of pepsin/HCl solution. After digestion, the pH of the solution was adjusted to 7.4 using NaOH and PBS. The solution was then lyophilized, ground into powder again, and stored at 4°C. For gelation, the powder was dissolved in PBS at a concentration of 20 mg/ml and incubated at 37°C. Scanning electron microscopy, swelling, and compression tests were performed to characterize the hydrogel.

Results: Following hydrogel preparation, some tests were conducted to evaluate its properties. SEM imaging revealed a pore diameter ranging from 50 to 65 µm and confirmed a uniform morphology. The hydrogel also exhibited favorable mechanical characteristics. The results of the swelling rate were included in the inflation percentage formula, and its rate was in the range of 500 to 1500 percent.

Conclusion: According to the results obtained, amniotic membrane hydrogel has good physical properties and is suitable for injectable scaffolds and bulk scaffolds, and can also be used for bone tissue engineering.

Keywords: Hydrogel, Amniotic Membrane-Based Hydrogel, Tissue Engineering

P-99: Alterations Expression of Key RNA Methylation (m6A) Enzymes in Testicular Tissue of Rats with Induced Varicocele

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Background: Epigenetic mechanisms are integral to male reproductive health and fertility, with RNA modifications particularly N6-methyladenosine (m6A) playing a critical role in RNA metabolism. Varicocele, a common contributor to male infertility, is closely linked to oxidative stress, which detrimentally affects sperm function.

Materials and Methods: In this experimental study, 15 male Wistar rats (age: 6–8 weeks; weight: 150–200 g) were randomly assigned to three groups: control, sham-operated, and varicocele-induced (n = 5 per group). Varicocele was surgically induced in the designated group. After eight weeks, tes-

testicular tissue and sperm samples were collected for analysis. Evaluations included assessment of sperm parameters and functionality, and analysis of gene expression related to RNA modification. Real-time quantitative reverse transcription PCR (qRT-PCR) was used to measure the expression of METTL3 (a writer), FTO (erasers), and YTHDF2 (a reader of m6A-modified RNA).

Results: Rats with induced varicocele exhibited notable histological abnormalities, including disorganized seminiferous tubules. Sperm analysis revealed significantly reduced concentration ($P=0.006$) and a higher percentage of abnormal morphology ($P=0.001$) in the varicocele group. Indicators of oxidative stress including increased elevated intracellular reactive oxygen species (ROS), and enhanced DNA damage were also observed. Furthermore, gene expression analysis demonstrated significant downregulation of METTL3 ($P=0.001$), FTO ($P=0.008$), and YTHDF2 ($P=0.006$) compared to the control group, suggesting impaired RNA modification pathways.

Conclusion: The study highlights the detrimental effects of varicocele on testicular morphology, sperm quality, and the expression of crucial RNA modification enzymes. These findings provide important insights into the molecular mechanisms of varicocele-associated male infertility and may aid in identifying potential therapeutic targets.

Keywords: Chromatin, Oxidative Stress, N6-Methyladenosine, Sperm, Varicocele

P-100: Effect of Intracerebroventricularly Administered NaHS on The Hippocampus in PCOS-Induced Rats

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Background: Polycystic ovary syndrome (PCOS) is a metabolic and endocrine disorder commonly observed in women of reproductive age. It is often associated with cognitive impairments due to increased oxidative stress and inflammation. This study aimed to evaluate whether intracerebroventricular (I.C.V) administration of sodium hydrosulfide (NaHS) could improve cognitive dysfunction in a rat model of PCOS.

Materials and Methods: Thirty female rats were randomly assigned to three groups: (1) Control, (2) PCOS, and (3) PCOS + NaHS. PCOS was induced by oral administration of letrozole (1 mg/kg) for 27 consecutive days. NaHS (17 μ g/4 μ l) was administered daily via I.C.V injection for one week to the PCOS + NaHS group. At the end of the experimental period, behavioral assessments including the Novel Object Recognition (NOR) test and Passive Avoidance Test (PAT) were performed. The right hippocampus was collected to evaluate levels of hydrogen sulfide (H_2S), malondialdehyde (MDA), and superoxide dismutase (SOD) activity.

Results: PCOS induction resulted in significant cognitive impairment and reduced performance in the passive avoidance task. It also increased oxidative stress and decreased H_2S levels in the hippocampus. Additionally, ovarian tissue analysis revealed an increased number of cysts. NaHS treatment significantly improved cognitive performance and passive avoidance behavior, as well as restored hippocampal H_2S levels and reduced oxidative stress.

Conclusion: Intracerebroventricular administration of NaHS may mitigate cognitive deficits in PCOS by enhancing hip-

pocampal H_2S levels and reducing oxidative stress.

Keywords: Polycystic Ovary Syndrome, Cognitive Impairment, Sodium Hydrosulfide, Hippocampus, Oxidative Stress

P-101: The Effect of Microvesicles Extracted from Follicular Fluid on The Quality of Human Sperm after Vitrification

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Background: The advancement of assisted reproductive technologies (ART) has been crucial for the treatment of infertility. Vitricification represents an innovative technique for sperm cryopreservation. Evidence suggests that follicular fluid (FF) and microvesicles derived from follicular fluid (MVs-FF) modulate sperm function, specifically motility and viability. The present study aimed to evaluate the effect of supplementing the vitrification medium with MVs-FF and FF.

Materials and Methods: The experimental procedure involved the isolation of MVs from FF, followed by the determination of FF and MVs concentrations and the characterization of extracted MVs in terms of size and morphology. Subsequently, these components were incorporated into the vitrification medium at concentrations of 50 mM and 100 mM for both FF and MVs-FF. Following thawing, assessments were conducted on sperm total and progressive motility, viability, plasma membrane integrity, DNA fragmentation, and the expression levels of apoptosis-related genes (*BAX* and *BCL2*).

Results: The results indicated that the lower concentration (50 mM) of MVs-FF led to significant improvements in sperm total and progressive motility, viability, and plasma membrane integrity compared to the control group ($P<0.05$), and also regulated the expression of genes associated with apoptosis. In contrast, only the higher concentration (100 mM) of FF demonstrated a significant effect.

Conclusion: These observations suggest that MVs derived from FF are more effective at enhancing post-thaw sperm quality at a lower concentration compared to FF alone.

Keywords: Microvesicle, Follicular Fluid, Vitricification, qPCR

P-102: Antral Follicle Formation in Human Vitricified Ovarian Fragments After one Week In Vitro Culture Stimulated with Follicular Fluid

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Background: According to the World Health Organization, infertility affects 12% of couples worldwide. In this regard, female fertility preservation through methods such as cryopreservation of the ovary and follicle culture is an important topic to investigate. Although limits to these approaches led scientists to examine new ideas. Human follicular fluid (FF) composition of hormones, fatty acids, and proteins is a key element for follicle development and oocyte maturation. The microenvironment provided by follicular fluid stimulates follicle activation and subsequent development.

Materials and Methods: In this research, human follicular fluid was added to the ovarian fragment culture medium as a supplement. The vitrified-warmed ovarian fragments (2.5×0.5×5 mm³) were cultured for one week in alpha-MEM, 1% ITS, 10% HAS, 0.5 IU/ml FSH, and 10% FF.

Results: Histological analysis on day0 and day7 revealed that the mean of follicle activation has meaningfully increased from 53.44% to 94.44% ($P \leq 0.0005$). Histological analysis also revealed the presence of morphologically healthy and growing antral follicles after 7 days of culture with follicular fluid stimulation. There were no preantral or antral follicles on day 0 of the fragments.

Conclusion: Our results suggest that supplementation of ovarian fragments in vitro culture with follicular fluid induces antral follicle formation.

Keywords: Follicular Fluid, Antral Follicle, Follicular Activation

P-103: The Effect of Empagliflozin on In Vitro Maturation of Immature Mouse Oocytes

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Background: *In vitro* maturation (IVM) is an artificial process and aims to start the oocyte internal mechanisms for completion of maturation *in vitro*. Calcium homeostasis that plays an important role in maturation is controlled by mitochondria as well, but during in vitro culture the gathering of oxidative stress becomes an obstacle for maturation and reduces the oocyte maturation rate. Empagliflozin is an antidiabetic drug, also has antioxidant properties and by increasing the total antioxidant capacity of the cell, prevents damage to the mitochondria, and with this action, it plays an effective role in maintaining calcium homeostasis.

Materials and Methods: In this research, we examined the effects of empagliflozin on IVM of mouse oocyte. Immature oocytes were mechanically isolated from 6-8 weeks old Naval Medical Research Institute (NMRI) mice and cultured in 30 µl droplets of MEM alpha media with 50 nM (E1), 100 nM (E2), 1 µM (E3) and 10 µM (E4) of empagliflozin doses and were incubated for 16-18 hours in an 37°C, 5% CO₂ incubator. The control group did not receive any empagliflozin (E0). After in-

cubation, IVM rate was assessed. Chi-square test was used to analyze the data.

Results: After 16-18 h, Maturation rate of oocytes in E1 group had meaningful difference in comparison to E0 group ($P \leq 0.05$).

Conclusion: Our findings show that empagliflozin is an effective element in oocyte in vitro maturation and it could affect oocytes in order to achieve MII in a phase dose depending manner, and it could be used as a supplement in oocyte culture media.

Keywords: *In vitro* Maturation, Empagliflozin, Mouse, Oocyte

P-104: Effect of Aflatoxin B1 on Testis Cell lines and Its Relationship with The Activation of Internal and External Pathways of Apoptosis and The Therapeutic Role of Taraxasterol

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Background: Aflatoxin is a fungal defense toxin produced by *Aspergillus flavus* and parasitic species. These fungi grow rapidly in cereals, legumes, and nutritious grains and secrete aflatoxin as a defense toxin. Taraxasterol, as an important bioactive compound in dandelion, has strong anti-inflammatory and antioxidant activity. purpose of this research is to investigate the effect of aflatoxin B1 on testis cell line and its relationship with the activation of internal and external pathways of apoptosis and the therapeutic role of Taraxasterol.

Materials and Methods: Testicular cell lines cultured in RPMI medium. MTT method was used to evaluate cell viability in the presence of 3.6 µM AFB1 concentration and different concentrations of taraxasterol and IC₅₀ was calculated. expression level of caspase 3, caspase 9 and caspase 8 genes was investigated by Real-Time PCR method and cell apoptosis was measured by tunnel staining.

Results: The results of the MTT test showed that the concentration of 3.6 µM of AFB1 decreased the survival rate of testicular cells, and in the presence of concentrations of 2.5, 5 and 10 µM Taraxasterol, respectively. Real-time PCR results also showed that the concentration of 3.6 µM AFB1 causes apoptosis of testicular cells by increasing the expression of caspase 3, caspase 9 and caspase 8 genes, and the concentration of 10 µM Taraxasterol causes the decrease of the expression of caspase 3, caspase 9 and caspase 8 genes. concentration of 3.6 µM of AFB1 increased the apoptosis, and it decreased in the presence of 10 µM concentration of Taraxasterol.

Conclusion: results of this study confirm the therapeutic role of taraxasterol in AFB1-induced cytotoxicity in a testicular cell line and may be considered a promising agent for the treatment of fertility problems in the future.

Keywords: Taraxasterol, Protective Effect, Apoptosis, AFB1, Testicular Cell Line

Epidemiology and Health

P-105: An Ethical Appraisal of Prenatal Screening for Adult-Onset Genetic Diseases

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Background: Screening tests are performed with the aim of distinguishing healthy embryos from those with defects: diseases or abnormalities. Some of the diseases that can be diagnosed at this time are diseases of genetic origin that manifest in adulthood. Huntington's disease, types of cancer, schizophrenia, coronary artery disease, cerebellar ataxia, diabetes, etc. fall into this group. One of the important questions in the ethical analysis of fetal screening is which diseases are permissible to screen for? That is, in general, does ethics allow screening for diseases that manifest in adulthood?

Materials and Methods: This research has been conducted on the basis of a moral-analytic method which is congruent with the nature of morality as a normative entity.

Results: Several important factors influence the provision of an answer to this question. (1) Does knowledge of the disease have any impact on the process of preventing, controlling or treating it, or is the only way to abort the defective embryo? (2) How severe is the disease and the pain and suffering that will be imposed on the patient in the future, and how long will it last? (3) How certain is the screening result; that is, what is the margin of error of the prediction by the test of the likelihood of the manifestation of the disease? (4) At what age does the disease occur?

Conclusion: We should add to these points that genetic testing is possible to diagnose these diseases at any time after the child is born until adulthood. Also, the genes that cause these diseases are passed from one generation to the next, so aborting fetuses carrying these genes can mean stopping the cycle of transmission of these diseases. Finally, providing counseling to parents and explaining all available options and the consequences of their choices is one of the duties of the medical staff and plays a very important role in informed decision-making by parents.

Keywords: Adult-Onset Genetic Diseases, Prenatal Screening, Ethics

Female Infertility

P-106: The Effect of Intravenous Remdesivir on Endometrial Receptivity in Female Mice

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Background: Coronavirus disease 2019 (COVID-19) continues to spread and cause serious health problems worldwide, so the investigation of drug therapies to reduce symptoms, disease recovery, and prevent death is necessary. Remdesivir (RDV)

is the first antiviral drug approved by the US Food and Drug Administration to treat COVID-19. While the overall safety of RDV has been studied, its adverse effects on the reproductive system are largely unknown. In mammals, the endometrium is a key organ for implantation, and maintaining its optimal conditions is essential for embryo maintenance and pregnancy success. Therefore, any damage to the endometrium can cause implantation failure. no study has been conducted to date on the effect of RDV on the implantation process and endometrial receptivity. Accordingly, in this study, we will investigate the effects of remdesivir on endometrial receptivity in pregnancy.

Materials and Methods: The drug was used at different doses of 2, 4, and 6 µm in the mice. After 10 days, adult female mice were mated with fertile males of the same strain to induce pregnancy. The morning after the vaginal plaque was found was considered gestation day 1 (GD). On day 4.5, female mice were euthanized. After that, tissue examinations were done by H&E staining. The expression of the inflammatory factors (IL6/IL1β) at the gene and protein levels, and the level of estrogen hormone in the serum of pregnant mice were measured.

Results: The results showed that RDV administration reduced pinopodes on the surface of the endometrium. The expression of IL-6 and IL1β increased at the gene and protein levels compared to the control group. The estrogen level in the serum of pregnant mice decreased after RDV administration compared to the control group.

Conclusion: pregnant mothers and women of their childbearing age should be warned about the use of RDV, and its side effects should be prevented.

Keywords: Remdesivir, Endometrium, Pinopodes, Inflammatory factors (IL6/IL1β), Estrogen

P-107: Managing Stress and Anxiety of Infertility in Women: A Review of Psychonursing and Midwifery Interventions

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Background: Infertility is a major reproductive health challenge, defined as the inability to conceive after one year of regular, unprotected intercourse. It has been associated with significant psychological consequences, including increased levels of stress, anxiety, and emotional distress. These psychological factors are not only outcomes of infertility but may also contribute to reduced chances of conception, indicating a bidirectional relationship.

Materials and Methods: To examine the effectiveness of psychological interventions—particularly cognitive-behavioral therapy (CBT)—in managing infertility-related stress, a systematic review was conducted. Literature searches were performed in reputable scientific databases, including PubMed, Google Scholar, and Medline. Keywords such as “infertility,” “stress,” “cognitive-behavioral therapy,” “coping strategies,” and “psychological interventions” were used. Studies published between 2020 and 2025 were selected for analysis and evaluation based on their relevance and methodological quality.

Results: Stress has been found to negatively affect fertility, and infertility itself is a major source of psychological distress, which can further reduce the success rates of treatment. Evidence suggests that CBT can effectively reduce stress and anxiety in infertile women, improve health-promoting behaviors, foster hope, and replace negative beliefs with more realistic and positive thoughts. These improvements may also contribute to higher pregnancy rates, especially in women undergoing assisted reproductive technologies (ART) with unexplained infertility.

Conclusion: Given the profound psychological burden of infertility, integrating psychological care—particularly psychonursing and midwifery interventions based on CBT—into infertility treatment programs is essential. These interventions can play a crucial role in alleviating anxiety, depression, and stress, thereby enhancing the overall well-being of infertile women and potentially improving treatment outcomes.

Keywords: Infertility, Stress, Cognitive-behavioral therapy, Psychological interventions, Coping strategies

P-108: Investigation of HSD3B, StAR, and CYP11A1 Proteins in Plasma Levels of Endometriosis Patients Treated with Dienogest

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Background: While progesterone resistance is associated with the pathology of endometriosis, many markers play a role in its pathway. Markers such as HSD3B, StAR, CYP11A1 are important in progesterone production. Since the progesterone currently prescribed for the treatment of endometriosis is dienogest, this study aimed to investigate the effect of dienogest on HSD3B, CYP11A1, and StAR markers.

Materials and Methods: Patients with endometriosis participating in this study received an oral dose of 2 mg dienogest per day for six months as prescribed treatment. Serum samples were collected from patients before and 6 months after dienogest administration and were used to measure HSD3B, StAR, and CYP11A1 concentrations. The patients' visual analog scale (VAS) of pain was recorded at both times.

Results: VAS score decreased significantly after receiving dienogest ($P < 0.05$). CYP11A1 decreased significantly after receiving dienogest ($P < 0.05$), and HSD3B, StAR increased significantly after receiving dienogest ($P < 0.05$).

Conclusion: Since the progesterone that is currently prescribed for the treatment of endometriosis is dienogest, the reduction in pain levels and plasma levels of CYP11A1 and the increase in plasma levels of HSD3B, StAR under the influence of dienogest indicate that this drug can affect progesterone production genes. Therefore, by identifying the molecular pathways in the effect of this drug, it is possible to help better treat endometriosis and offer the potential for innovative treatments.

Keywords: Dienogest, HSD3B, StAR, CYP11A1, Pain

P-109: Determining Factors Associated with The Number of Oocytes with Appropriate Morphology in Infertile Women

Referring to The Royan Institute

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Background: This study aimed to identify factors that influence the number of morphologically normal oocytes (MNO), which enhance the success rate of assisted reproductive interventions.

Materials and Methods: In this cross-sectional study, zero-inflated Poisson (ZIP) regression and semiparametric zero-inflated negative binomial (SZINB) regression were used to model count data with many zeros, involving 950 infertile women referring to an infertility center in Tehran, Iran.

Results: After adjusting for confounding factors, the findings indicated that ovarian surgery history ($P = 0.045$) and the presence of disorders in either the ovary status (right or left) ($P = 0.041$) were significantly associated with a reduced number of MNO. Additionally, older maternal age ($P = 0.038$), an increased LH/FSH (luteinizing hormone (LH) / follicle-stimulating hormone (FSH)) ratio ($P = 0.044$), elevated thyroid-stimulating hormone (TSH) levels ($P = 0.026$), and higher fasting blood sugar (FBS) levels ($P = 0.049$) were all inversely associated with MNO. Higher hirsutism scores ($P = 0.049$) also had a negative impact on MNO. Furthermore, an increased number of ART cycles ($P = 0.037$) exhibited a nonlinear inverse relationship with MNO.

Conclusion: The results of this study may enable us to predict the number of eligible women receiving assisted reproductive technology, thus supporting the medical team and infertile women in making informed decisions. Additionally, the findings underscore the importance and necessity of applying nonlinear models in clinical research.

Keywords: Morphologically Normal Oocytes, Infertile Women, Zero-Inflated Models (ZI)

P-110: The Role of the STAT3 Signaling Pathway in Patients with Recurrent Pregnancy Loss: A Systematic Review

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Background: Given the role of signal transduction and transcription activator 3 (STAT3) in biological processes such as proliferation, differentiation, and inflammation, its importance in the reproductive tract, especially during pregnancy, is undeniable. STAT signaling is essential for controlling embryonic implantation and endometrial decidualization during pregnancy, ensuring the building and preservation of maternal-fetal immune tolerance.

Materials and Methods: We searched the keywords STAT3 and RPL across multiple databases, including PubMed, Scopus, and Google Scholar, spanning the years 2017 to 2025. The inclusion criteria encompassed studies performed in vitro, in vivo, and under clinical conditions that assessed the role of STAT3 in RPL. Data extraction focused on the therapeutic ramifications of STAT3 and the mechanisms through which STAT3 influences RPL.

Results: Research from 13 analyzed papers demonstrates that STAT3 activity in maternal and fetal tissues correlates with enhanced decidualization, trophoblast cell migration, and maternal and fetal immunological tolerance. Therefore, targeting the STAT3 signaling pathway could be an effective approach for the prevention and treatment of RPL. Consequently, inhibiting the STAT3 signaling pathway may serve as a viable strategy for the prevention and treatment of RPL. Promising findings have been shown in preclinical investigations; however, their efficacy remains unverified in clinical contexts.

Conclusion: In most female infertility, STAT3 expression is associated with a high rate of miscarriage. Preclinical studies showed the significant effectiveness of drugs targeting the STAT3 signaling pathway in treating RPL. Therefore, this pathway is a potential therapeutic target in infertility.

Keywords: STAT3, RPL, Pregnancy Complication, Miscarriage

P-111: The Effect of A Social Support Mobile Application on The Mental Health of Women after Miscarriage

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Background: Miscarriage frequently results in psychological distress, often exacerbated by limited access to supportive care in specific cultural and geographic contexts. Mobile health technology offers a confidential, accessible, and cost-effective platform to enhance psychological and social support following miscarriage. This study aimed to evaluate the impact of a mobile application designed to provide social support on the mental health of women after miscarriage.

Materials and Methods: A quasi-experimental design with a pretest-posttest control group was employed involving 36 women with a history of miscarriage before 20 weeks of gestation, recruited from comprehensive health centers in Shahrekord. Participants were randomly allocated to intervention and control groups. The intervention group utilized a social support mobile application offering online clinical services and peer group support in addition to routine care for one month, where-

as the control group received routine care only. Mental health outcomes were assessed using the General Health Questionnaire-28 (GHQ-28) at baseline, immediately post-intervention, and one month thereafter. Data were analyzed using appropriate inferential statistics.

Results: Independent t-tests revealed no significant baseline differences in social functioning scores between groups ($P=0.07$). Analysis of covariance (ANCOVA) demonstrated significant improvements in the intervention group immediately and one month post-intervention compared to controls ($P<0.001$). Repeated measures analysis confirmed significant within-group improvements over time in both groups, with greater gains observed in the intervention group ($P=0.03$ for control; $P<0.001$ for intervention), indicating a positive effect of the mobile application on social functioning.

Conclusion: The mobile-based social support application significantly enhances mental health and social functioning in women after miscarriage by providing multifaceted support and empowerment. Integrating this technology into community mental health programs is recommended to improve access to care.

Keywords: Application, Social support, Mental health, Miscarriage

P-112: Evaluating The Effectiveness of Probiotic Consumption in Women with PCOS Candidates for Intrauterine Insemination: A Randomized Double-Blind Clinical Trial

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Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting approximately 15% of women of reproductive age, often leading to infertility due to ovulation disorders. Recent studies suggest that gut microbiome dysbiosis may play a key role in PCOS pathogenesis. Probiotics have shown potential in improving metabolic parameters and reproductive outcomes. This study aimed to evaluate the effectiveness of probiotic supplementation in PCOS patients undergoing intrauterine insemination (IUI).

Materials and Methods: This randomized, double-blind, placebo-controlled clinical trial included 100 women aged 19-37 years with PCOS (diagnosed according to Rotterdam 2003 criteria) who were candidates for IUI at Kowsar Hospital Infertility Center. Participants were randomly allocated to intervention ($n=50$) and placebo ($n=50$) groups. The intervention group received oral probiotic capsules (Lactofem, containing 7 bacterial strains) daily for one month, followed by ovulation induction drugs plus probiotics in the second month. The placebo group received identical-appearing placebo capsules. Primary outcomes included chemical and clinical pregnancy rates. Secondary outcomes included dominant follicle count and endometrial thickness.

Results: Mean patient age was 28.7 ± 4.9 years. No significant differences were observed between groups regarding baseline demographic and paraclinical parameters ($p>0.05$). Chemical pregnancy rate was higher in the probiotic group compared to placebo (16% vs. 12%), but the difference was not statistically significant ($P=0.564$). Clinical pregnancy rate was significantly

higher in the probiotic group compared to placebo (14% vs. 4%; $P=0.008$). Endometrial thickness showed significant improvement in the intervention group ($P=0.028$).

Conclusion: Probiotic supplementation with Lactofem capsules for 8 weeks in PCOS patients undergoing IUI significantly improved clinical pregnancy rates and endometrial thickness compared to placebo. These findings suggest that probiotics may be a beneficial adjuvant therapy for improving reproductive outcomes in PCOS patients undergoing assisted reproductive techniques.

Keywords: Polycystic Ovary Syndrome, Probiotics, Intrauterine insemination, Infertility, Assisted Reproductive Technology

P-113: Five-Year Systematic Review of Endometriosis and Its Impact on Reproductive Health Outcomes

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Background: Endometriosis is a chronic and often debilitating gynecological disorder affecting approximately 10% of women during their reproductive years. The condition occurs when endometrial-like tissue grows outside the uterine cavity, leading to chronic pelvic pain, severe dysmenorrhea, and infertility. Beyond physical symptoms, endometriosis profoundly impacts mental health and overall quality of life. Given its prevalence and multifaceted consequences, understanding the relationship between endometriosis and reproductive health outcomes is critical for developing effective treatment strategies and improving patient counseling.

Materials and Methods: This systematic review analyzed studies published between 2018 and 2023, sourced from major databases including PubMed, Cochrane Library, and Embase. The selection criteria focused on peer-reviewed articles investigating endometriosis's effects on fertility, pregnancy outcomes, and quality of life. Two independent reviewers conducted data extraction and assessed study quality using the Newcastle-Ottawa Scale to ensure methodological rigor.

Results: 1. Fertility Implications: - Endometriosis significantly reduces fertility rates due to mechanisms such as ovarian dysfunction, distorted pelvic anatomy, and hormonal imbalances. - Assisted reproductive technologies (ART) offer varying success rates, with emerging evidence suggesting that surgical excision of endometriotic lesions before ART may enhance outcomes. 2. Pregnancy Risks: - Women with endometriosis face elevated risks of adverse pregnancy outcomes, including miscarriage, preterm birth, and ectopic pregnancy. These complications are attributed to inflammatory changes and structural abnormalities in the reproductive tract. - Current guidelines recommend specialized prenatal care for these patients to mitigate risks. 3. Quality of Life: - The chronic pain and emotional toll of endometriosis lead to substantial declines in quality of life, affecting daily activities, work productivity, and mental health. - Multidisciplinary care models integrating pain management, psychological support, and patient education are vital for holistic treatment.

Conclusion: Endometriosis remains a major challenge in reproductive health, with far-reaching effects on fertility, pregnancy, and overall well-being. A comprehensive, patient-centered approach—combining medical, surgical, and psychosocial interventions—is essential to address this complex condition. Future

research should prioritize longitudinal studies to refine treatment protocols and improve long-term outcomes for affected women.

Keywords: Endometriosis, Reproductive Health, Pregnancy complications, Quality of life, Chronic pain

P-114: Five-Year Systematic Review on the Management and Treatment of Recurrent Miscarriage

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Background: Recurrent miscarriage, defined as the loss of three or more consecutive pregnancies, affects approximately 1-2% of women of reproductive age. This condition not only poses significant emotional distress but also raises concerns regarding underlying health issues. The purpose of this systematic review is to analyze the latest research over the past five years regarding the management and treatment strategies for recurrent miscarriage, focusing on diagnostic evaluations, therapeutic interventions, and patient outcomes.

Materials and Methods: This systematic review was conducted following PRISMA guidelines. A comprehensive literature search was performed in databases such as PubMed, Cochrane Library, and Embase for studies published between 2018 and 2023. Inclusion criteria encompassed peer-reviewed articles addressing the management and treatment of recurrent miscarriage, including diagnostic evaluations, medical and surgical treatments, and lifestyle modifications. Data extraction and quality assessment were carried out independently by two reviewers using the Newcastle-Ottawa Scale.

Results: 1. Etiology of Recurrent Miscarriage: • The review identified several common causes, including chromosomal abnormalities (up to 50% of cases), uterine anomalies, hormonal disorders, autoimmune factors, and thrombophilia. Genetic testing of products of conception remains crucial for identifying chromosomal issues. 2. Diagnostic Approaches: • A comprehensive evaluation is essential. Recommended assessments include karyotyping, hysterosalpingography, and testing for antiphospholipid syndrome and thyroid dysfunction. Recent studies emphasize the importance of a multidisciplinary approach to diagnosis. 3. Management Strategies: • Treatment varies based on the identified cause. Hormonal treatments, particularly progesterone supplementation, are frequently utilized. For women with antiphospholipid syndrome, low-dose aspirin and heparin have shown positive outcomes in preventing miscarriage. 4. Surgical Interventions: • Surgical options, such as hysteroscopic surgery for uterine anomalies, can improve reproductive outcomes. Recent evidence suggests that addressing anatomical issues significantly enhances the chances of a successful pregnancy. 5. Lifestyle Modifications: • Lifestyle factors, including smoking cessation, weight management, and dietary changes, are associated with improved pregnancy outcomes. The review highlights the need for counseling on lifestyle modifications as part of comprehensive care.

Conclusion: Recurrent miscarriage is a multifaceted condition requiring individualized management strategies. Early diagnosis and tailored treatment plans based on identified causes are essential for improving pregnancy outcomes. This review underscores the importance of a holistic approach, combining medical, surgical, and lifestyle interventions. Future research

should focus on standardizing guidelines and exploring new therapeutic options to enhance care for women experiencing recurrent miscarriage.

Keywords: Recurrent Miscarriage, Antiphospholipid Syndrome, Lifestyle Modifications, Hysterosalpingography

P-115: The Trends in Polycystic Ovary Syndrome-related Infertility: A Bibliometric Analysis

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Background: Polycystic ovary syndrome (PCOS) is a leading cause of anovulatory infertility, significantly impacting women's reproductive health. Effective management demands multidisciplinary strategies integrating hormonal, metabolic, and lifestyle interventions to address its heterogeneous manifestations. Hence, bibliometric analysis could provide a comprehensive landscape of the infertility concerns in PCOS research, guiding scientists and clinicians in shaping future investigations and evidence-based therapies.

Materials and Methods: We searched the Scopus database using the MeSH-expanded "PCOS" and "infertility" terms in the document's title, abstract, and keywords to extract the reports that studied infertility and PCOS. Then, papers in the English language that were published between 2000-2025 were selected to be processed via the Bibliometrix package (R software) and VOSviewer for network analysis, while PowerBI software was used to generate temporal visualizations.

Results: In this study, 5,081 articles authored by 22,289 researchers with 26,254 affiliations across 168 countries were analyzed using the Scopus database. The findings identified the United States, the Royan Institute's Department of Endocrinology and Female Infertility, and Dr. Richard S. Legro as the most productive country, institute, and author, respectively. The co-occurrence network of 618 keywords used by authors revealed 15 clusters; however, the co-occurrence of all keywords in the papers revealed 4 different clusters.

Conclusion: The analysis of co-occurring keywords identified 15 dimensions based on the authors' keywords, which were then compared into four main categories derived from the keywords in the papers: Pathophysiology (genes/hormones), Clinical Interventions (ART/medications), Comorbidities (inflammation/mental health), and Management (lifestyle and emerging technologies). From 2000 to 2010, research predominantly focused on clinical interventions and pathophysiology. However, in the 2010s, attention shifted to metabolic comorbidities and precision medicine, incorporating innovations such as AI and the gut microbiome. This trend highlights an increasing integration of technological and holistic management approaches in PCOS and infertility research, emphasizing the importance of precision medicine that combines genetic, metabolic, and patient-centered insights.

Keywords: PCOS, Infertility, Bibliometric, Network analysis, AI

P-116: To Evaluate The Reproductive Outcome in Patients with Isthmocele after Previous Cesarean Section in Art Cycles

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Background: The cesarean section rate is progressively increasing all over the world. One of the most common gynecologic complications of cesarean section is poor uterine scar healing, known as an isthmocele. This study aimed to evaluate the reproductive outcomes of assisted reproductive techniques cycles and first-trimester pregnancy complications in patients with isthmocele with previous cesarean section.

Materials and Methods: In this retrospective cohort study, 215 women with secondary infertility undergoing ART cycles participated from April 2019 to April 2023. Reproductive outcomes of cycles of patients with a history of one or more previous CS with hysterosonography visible isthmocele (n=173) were compared to those of patients with a history of at least one delivery (over 24 weeks) either naturally or cesarean section without isthmocele in our infertility clinic during the same period. The isthmocele group was also divided into three grades according to Gubbini et al.'s classification. The primary outcome measure was clinical pregnancy rate. Secondary outcome measures were implantation rate, abortion rate, ectopic pregnancy, ongoing pregnancy rate, and live birth rate.

Results: Although there was no statistically significant difference between the cumulative clinical pregnancy rate of two consecutive cycles between groups, the cumulative clinical pregnancy rate of fresh embryo transfer cycles was lower in the isthmocele group than the control group (P=0.031). The cumulative rates of implantation, ectopic pregnancy, abortion, and live birth of two consecutive cycles were comparable between groups.

Conclusion: The pregnancy rate is reduced following fresh embryo transfer in women with a history of Cs with isthmocele. Further prospective studies with larger populations are needed to support and confirm this.

Keywords: Isthmocele, Cesarean, Reproductive Outcomes, Assisted Reproductive Techniques

P-117: The Effect of Ovarian Stimulation Drugs on Peripheral Blood T CD8+ Cells in Women with Endometriosis Undergoing ART Cycles

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Background: Endometriosis is defined by the presence of en-

dometrial like tissue outside the uterine cavity. Although the exact cause of endometriosis remains uncertain, hormonal, genetic, and immunological factors are implicated in its pathogenesis. Only a limited number of studies have explored changes in cytotoxic T cells in endometriosis. In addition, the alterations of these cells and the effect of GnRH analogue drugs on them remain unclear in endometriosis. So, the aim of this study is to evaluate the effect of ovarian stimulation drugs, GnRH agonist and antagonist, on peripheral blood T CD8⁺ cells in women with endometriosis undergoing assisted reproductive technology (ART).

Materials and Methods: In this cohort study, forty infertile women with endometriosis will participate in the ovarian stimulation in IVF/ICSI cycles at the Royan Infertility Clinic. Eligible women consist of women under 40 years old, with a BMI below 35 kg/m², affected by endometriosis confirmed by laparoscopy or ultrasonography, undergoing their first IVF, or who have at least a three-month interval since their last cycle. Exclusion criteria are autoimmune diseases, untreated endocrine diseases, and poor ovarian response. The percentage of CD8-positive cells in peripheral blood mononuclear cells (PB-MCs) was assessed by flow cytometry using anti-human CD3 and anti-human CD8 antibodies on days 2 to 3 of the menstrual cycle and on the day of ovarian puncture.

Results: 15 endometriosis women were included between 31 Dec 2024 and 26 Apr 2025. Peripheral blood samples were collected from 9 women on the starting day of the ovarian stimulation cycle and 6 women on ovarian puncture day. the percentage of the peripheral blood T CD8⁺ cells was not statistically different between the starting day and the puncture day.

Conclusion: In the current sample size, no significant changes were seen in the frequency of peripheral blood T cytotoxic cells. The conclusion will be drawn after enrollment of 40 women in this study.

Keywords: Endometriosis, CD8⁺ T Cell, Peripheral Blood, Assisted Reproductive Technology

P-118: A Review of Hormonal and Biological Therapies for Endometriosis: Latest Developments

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Background: Endometriosis is a chronic, benign estrogen-dependent disease characterized by the presence of endometrial glands and stroma outside the uterine cavity. new drugs are under investigation for the treatment of endometriosis. This review aims to give the reader a complete and updated overview of hormonal and biological therapies for the treatment of endometriosis.

Materials and Methods: The study reviewed several significant articles in the field between 2010 and 2025. Reviews in the journal and PubMed, Science Direct, Elsevier, ProQuest, Willy, Springer, and Google Scholar databases with keywords Elagolix, aromatase inhibitors, gonadotropin-releasing hormone antagonists, hormonal treatments, and biological therapy. The results were analyzed and ranked schematically. For statistical

analysis, statistical tests were used.

Results: Among the new drugs investigated, late clinical trials on gonadotropin-releasing hormone (GnRH) antagonists and aromatase inhibitors (AIs) have demonstrated the most promising results. For this reason, elagolix, a new GnRH antagonist, recently received approval from the Food and Drug Administration (FDA) for treating pain associated with endometriosis. Other drugs with innovative targets have been identified, but the majority of these compounds have only been evaluated in pre-clinical studies or early clinical trials.

Conclusion: Thus, further extensive clinical research is necessary to better elucidate their pharmacologic characteristics, their efficacy, and safety for the treatment of this benign chronic disease.

Keywords: Elagolix, Aromatase Inhibitors, Gonadotropin-Releasing Hormone Antagonists, Hormonal Treatments, Biological Therapy

P-119: Ectopic Pregnancy Risk in Fresh and Frozen Embryo Transfers: Cleavage vs. Blastocyst vs. Sequential

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Background: Assisted reproductive technology (ART) offers effective infertility treatment but also raises the likelihood of ectopic pregnancy (EP). With EP rates climbing and maternal morbidity a pressing concern, clinicians must identify the transfer stage that carries the smallest risk. The clinical relevance of this information extends to patient counselling and protocol design.

Materials and Methods: This retrospective cross-sectional analysis reviewed electronic medical records collected with Rasha software from 2015 to 2020. Among 21,203 embryo-transfer cycles, 7,658 clinical pregnancies produced 131 EPs. Investigators retrieved relevant variables from EP files and analysed them with SPSS v25. Statistical testing included one-way analysis of variance (ANOVA), χ^2 tests for categorical variables, and odds-ratio calculations performed in MedCalc; P<0.05 indicated statistical significance.

Results: EP occurred in 1.71 % of all transfers—1.43 % in frozen and 2.10 % in fresh cycles. In fresh cycles, cleavage-stage transfers showed the lowest EP rate (1.7 %), whereas sequential transfers showed the highest (4.7 %). In frozen-embryo transfers (FET), blastocyst- and cleavage-stage transfers each showed the lowest rate (1.4 %), with sequential transfers again showing the highest (1.9 %). Compared with frozen cycles, fresh cycles yielded odds ratios of 1.99 for cleavage, 0.95 for blastocyst, and 0.71 for sequential transfers.

Conclusion: Both fresh and frozen transfers carried an EP risk in this cohort, and the developmental stage at transfer influenced that risk. Cleavage- or blastocyst-stage FETs produced the fewest EPs. Selecting embryos at these stages and refining transfer protocols may help lower EP incidence in future ART

practice.

Keywords: Ectopic Pregnancy, Embryo Transfer, Blastocyst, Cleavage

P-120: Assessing The Risk of Cerebral Palsy in Offspring Conceived Through Assisted Reproductive Technology: A Systematic Review

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Background: Assisted Reproductive Technology (ART) includes procedures like *in vitro* fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI) that help fertility. Cerebral palsy (CP) is a group of chronic movement disorders arising early in development. The objective of reviewing the ART and CP relationship is to determine if such technology increases CP risk in offspring.

Materials and Methods: This review critically assesses 16 articles (2020-2025). Included were quantitative studies, meta-analyses, original articles, and systematic reviews. Full-text availability was the inclusion criterion; case studies were excluded. Articles were searched via systematic searching of PubMed, Scopus, Web of Science, and Google Scholar.

Results: Studies reveal that CP is at higher risk among ART-born infants than among naturally conceived children. For example, a 2020 meta-analysis, reviewing 10 studies, stated that ART carried a 1.82-fold increased risk for cerebral palsy. There was a 1.51-fold increased risk in another study. However, this increased risk is especially due to multiple pregnancy and preterm delivery, which are more common among ART pregnancies. When these factors are controlled for, particularly in analyses restricted to singleton, term births, the risk of CP above predicted either significantly diminishes or is canceled out altogether.

Conclusion: While a statistical correlation between ART and cerebral palsy risk has been established, a considerable portion of this risk appears to be explained by such conditions as prematurity and multiple births, which occur more commonly in ART pregnancies. There is also evidence of a declining incidence of CP over time following ART, which can be anticipated to be a consequence of shifting clinical practice, such as reducing multiple embryo transfer and improving neonatal care. Therefore, although it is important to closely monitor the health of infants conceived through ART, the risk of CP is less directly associated with the process of ART than with pregnancy complications.

Keywords: Assisted Reproductive Technology, Cerebral Palsy, Movement Disorders

P-121: Therapeutic Potential of Menstrual Blood-Derived Extracellular Vesicles for Female Infertility: An Advanced Systematic Review

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Background: Female infertility, particularly arising from pre-

mature ovarian insufficiency, endometrial dysfunction, and diminished ovarian reserve, represents a significant clinical challenge. While assisted reproductive technologies have improved outcomes, regenerative strategies capable of restoring intrinsic reproductive function remain limited. Extracellular vesicles (EVs) derived from menstrual blood stromal/stem cells (MenSCs) offer a promising, cell-free, and ethically acceptable therapeutic alternative due to their immunomodulatory and regenerative properties.

Materials and Methods: A systematic review was conducted according to PRISMA guidelines. Relevant studies were retrieved from PubMed, Scopus, and Web of Science up to April 2025. Eligible studies included preclinical and clinical investigations of MB-EVs targeting ovarian or endometrial dysfunction. Data were extracted on EV isolation, characterization, delivery, outcomes, and molecular mechanisms. Study quality and bias were assessed using standard tools.

Results: Fourteen studies met the inclusion criteria. MB-EVs were isolated primarily by ultracentrifugation and exhibited key exosomal markers (CD63, CD81, TSG101). In ovarian models, MB-EVs improved folliculogenesis, hormone levels, and estrous cycles. In endometrial models, they enhanced regeneration, angiogenesis, and receptivity. EV cargo, including miR-21, miR-126, and miR-29a, modulated PI3K/AKT, Wnt/ β -catenin, and TGF- β /Smad signaling, reducing apoptosis and fibrosis.

Conclusion: MB-EVs present a novel and accessible approach to restoring ovarian and endometrial function in female infertility. Their regenerative potential and safety profile support further clinical investigation, pending standardization of protocols and validation in human trials.

Keywords: Menstrual Blood, Female Infertility, Extracellular Vesicles, Ovarian Function, Endometrial Repair

P-122: Studying The Relationship Between Minimal Fetal Fraction and The Incidence Of Preeclampsia: A Limited Study

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Background: Preeclampsia is one of the important complications of pregnancy. Preeclampsia may be associated with low fetal fraction. Fetal fraction is the amount of fetal DNA in the NIPT (Noninvasive Prenatal Testing). Perhaps we can predict the occurrence of preeclampsia earlier by considering the minimum fetal fraction.

Materials and Methods: In this study, 70 pregnant mothers aged 25 to 40 years who needed to undergo NIPT testing and whose NIPT was within the minimum range of fetal fraction were included. This group was compared with the 100 cases of pregnant mothers who had NIPT within the normal fetal fraction range. The minimum fetal fraction was considered to be 5 to 6 percent. The age range of these mothers was also considered to be between 25 and 40 years. Both groups had singleton pregnancies and no underlying hypertension or other underlying disease. The pregnancy outcome of both groups was compared in terms of the incidence of preeclampsia.

Results: Of the 70 cases with a minimum fetal fraction, 8(11.4%) developed preeclampsia in the third trimester, but

only three (3%) cases in the control group developed preeclampsia.

Conclusion: It may be possible to predict the occurrence of preeclampsia by examining fetal fraction.

Keywords: Fetal Fraction, Preeclampsia, NIPT

P-123: Psychological Health of Women with Polycystic Ovary Syndrome and Associated Factors: A Report from The Babol Polycystic Ovary Syndrome Registry

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Background: Polycystic ovary syndrome (PCOS) is a common endocrine and reproductive disorder with an unclear etiology, influenced by genetic and environmental factors. While associated with anxiety and depression, little is known about other mood disorders. This study aims to explore the clinical features of PCOS and its related psychological issues.

Materials and Methods: This cross-sectional study utilized data from the Babol Polycystic Ovary Syndrome Registry (BP-COSR), which records women diagnosed with PCOS in Babol. The sample included 212 women who visited the Fatemeh Zahra Infertility Center between 2018 and 2024. Diagnoses were made according to the Rotterdam 2003 criteria by experienced gynecologists. Data on PCOS features and health outcomes were recorded by experts. Psychological status was assessed using the SCL-25 questionnaire, and hirsutism severity was evaluated with the Freeman-Galwey scoring system, with scores above 8 indicating significant hirsutism.

Results: Overall, 31.6% (n=67) of women with PCOS exhibited psychological disorders. Interpersonal sensitivity and obsessive-compulsive disorder were the most prevalent disturbances. The mental health of women with PCOS was significantly affected by the severity of hirsutism ($P=0.043$), acanthosis nigricans ($P=0.006$), hoarseness of voice ($P<0.001$), hair loss ($P<0.001$), waist circumference ($P=0.040$), hip circumference ($P=0.021$), and weight ($P=0.044$). Hirsutism and physical appearance variations may negatively impact body image and self-esteem, potentially leading to chronic stress and reduced mental well-being.

Conclusion: Based on these findings, comprehensive treatment should address both physical and psychological aspects of PCOS, including psychological counseling and support therapies alongside physiological management.

Keywords: Polycystic Ovary Syndrome, Psychological Health, Psychological Health, Mental Health

P-124: Altered Gene Expression of IL-18 and IL-18 Binding protein in The Endometrial Tissues of Women With Endometriosis

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Background: Endometriosis is a chronic inflammatory disease involving the growth of endometrial-like tissue outside the uterus. Although exact pathogenesis of endometriosis is unknown, dysregulations of different cytokines is reported in its pathogenesis. Interleukin 18 (IL-18) is a member of IL-1 family with proinflammatory properties. IL18 signaling is mediated through IL-18 receptor complex (IL18-R1, IL18-R2) while IL-18 binding protein (IL18-BP) is its natural inhibitor.

Objective: This study aimed to evaluate gene expression levels of IL-18, its receptors and IL-18BP in endometrial tissue of women with endometriosis in compare to controls.

Materials and Methods: In this ongoing case-control study, 30 women who underwent diagnostic laparoscopy will be enrolled (15 women with endometriosis and 15 women without endometriosis). Inclusion criteria consists of age between 20-45, regular menstrual cycles and not receiving hormonal drugs in the past 3 months. Ectopic endometrial samples from endometriosis group are obtained during laparoscopy while eutopic endometrial samples and endometrial samples of control group are collected with a pipelle. After tissue samples collection, RNA extraction and cDNA synthesis is performed. Gene expression are examined using real-time RT-PCR and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as housekeeping gene. The ANNOVA Kruskal-wallis test is used to data analysis.

Results: Till now, 11 women with endometriosis and 15 women without endometriosis were enrolled. The expression of IL-18, its receptors and IL18BP gene were significantly different between three endometrial tissue groups (eutopic and ectopic tissues of endometriosis women and normal endometrium tissues of control women) (IL18: P value =0.003; IL18R1: P value=0.017 ; IL18R2: P value=0.001 ; IL18BP: P value=0.0005).

Conclusion: It seems overexpression of IL18, its receptors (IL18R1 & IL18R2), its regulator (IL18BP) genes may contribute to impaired inflammatory responses and progression of endometriotic lesions. This imbalance may play a role in the development of a chronic inflammatory environment in endometriosis.

Keywords: Endometriosis, IL-18, IL-18 receptors, IL-18 Binding protein (IL18BP), Gene Expression.

P-125: Timing of Endometrial Injury in the Menstrual Cycle: A Randomized Controlled Trial Comparing Follicular and Luteal Phases in Women with Repeated Implantation Failure

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Background: Repeated implantation failure (RIF) is one of the major challenges in assisted reproductive technology (ART). Endometrial injury has been suggested as a potential strategy to improve endometrial receptivity and implantation. However,

the optimal timing of this intervention remains unclear. This study aimed to compare the effect of endometrial scratching performed during the follicular versus the luteal phase on pregnancy outcomes in women with RIF.

Materials and Methods: In this randomized controlled trial, 78 women with a history of at least one failed IVF cycle were randomly assigned to undergo endometrial injury using pipelle biopsy in either the follicular (n=38) or luteal phase (n=40) of the menstrual cycle preceding embryo transfer. Clinical, chemical, and ongoing pregnancy rates, as well as implantation rates, were compared between groups.

Results: No statistically significant differences were observed in pregnancy outcomes between the two groups. Chemical pregnancy occurred in 21.42% of the follicular group and 19.99% of the luteal group. Clinical pregnancy rates were 20% in both groups, and ongoing pregnancy occurred in 17.13% vs. 14.28%, respectively. Implantation rates were also similar (0.21 ± 0.28 vs. 0.17 ± 0.27 ; $P > 0.05$).

Conclusion: Our findings indicate that the timing of endometrial injury—whether in the follicular or luteal phase—does not significantly impact implantation or pregnancy outcomes in women with repeated implantation failure. Further research in larger and more stratified populations is recommended to identify subgroups who may benefit from this intervention.

Keywords: Endometrial Injury, Follicular Phase, Luteal Phase, Repeated Implantation Failure

P-126: The Role of Anti-Müllerian Hormone in Insulin Resistance and Hormonal Imbalance in Polycystic Ovary Syndrome

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Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women of reproductive age. It is characterized by hormonal imbalances, irregular menstrual cycles, hyperandrogenism, and insulin resistance. Despite its high prevalence, the exact cause of PCOS remains unclear. This study investigated the relationship between anti-müllerian hormone with insulin resistance and reproductive hormones in women with this syndrome.

Materials and Methods: A total of 100 women aged 18 to 45 years, including both healthy individuals and those diagnosed with PCOS, participated in this study. The diagnosis of PCOS was confirmed by a gynecologist based on clinical examination and transvaginal or pelvic ultrasound findings. For all participants, the following parameters were recorded: age, weight, height, waist circumference, hip circumference, fasting blood glucose, insulin levels, and serum concentrations of luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen, progesterone, free testosterone, and anti-Müllerian hormone (AMH).

Results: In this study, no significant difference was found in age or FSH levels between groups. Women with PCOS had higher BMI, LH, free testosterone, AMH, and insulin resistance, but lower estradiol and progesterone. AMH showed no significant correlation with LH, FSH, testosterone, or progesterone in either group. However, AMH correlated positively with estradiol in controls and negatively in PCOS patients.

Conclusion: Women with PCOS often experience overweight,

obesity, and hormonal imbalances. In healthy individuals, there is a positive and natural correlation between AMH and estradiol. In PCOS patients, this correlation is negative, indicating disruption in the HPO axis and abnormal folliculogenesis. This dysfunction can lead to anovulation and the accumulation of immature follicles. Early monitoring of AMH may help prevent reproductive and metabolic complications.

Keywords: Anti-Müllerian Hormone, Polycystic Ovary Syndrome, Insulin Resistance, Reproductive Hormones

P-127: Overview of The Synergistic Impact of HPV Infection and G. Vaginalis on Infertility

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Background: Human Papillomavirus (HPV) and Gardnerella vaginalis (G. vaginalis) are prevalent infections with significant implications for women's fertility. HPV is linked to infertility and cervical cancer, while abnormal levels of Gardnerella can lead to inflammation and chronic infections, complicating reproductive health. This review examines their simultaneous effects on infertility in women.

Materials and Methods: This systematic review was conducted in February 2025 and involved five stages: formulating the research question, executing a comprehensive literature search, extracting relevant studies, selecting articles, and reporting results. Searches were performed using keywords in databases such as PubMed, Magiran, Iran Doc, Science Direct, and Google Scholar. The initial search identified 315 articles; after applying inclusion and exclusion criteria per the PRISMA 2020 flow diagram, 14 studies published between 2021 and 2025 were included. The Newcastle-Ottawa Scale checklist evaluated study quality, yielding scores of 8 (5 studies), 7 (6 studies), and 6 (3 studies). Data were organized based on biological factors, immune system disorders, and psychosocial impacts.

Results: This review revealed several key complications linked to HPV and G. vaginalis infections, categorized into three areas: 1. Biological Factors: - Inflammation and Tissue Damage: HPV and G. vaginalis infections cause inflammation in genital tissues, impairing fertility and increasing risks. Chronic inflammation can lead to anatomical changes that hinder conception. - Altered Gamete Quality: These infections disrupt the quality of eggs and sperm, raising infertility rates. 2. Immune System Disorders: - Dysregulated Immune Response: G. vaginalis can induce an abnormal immune response, increasing the risk of recurrent HPV infections. - Vaginal Microbiome Disturbance: G. vaginalis-induced bacterial vaginosis alters the vaginal microbiome, influencing HPV infection rates and heightening infertility risks. 3. Psychological and Social Factors: - Mental Health Impact: Chronic infections adversely affect mental health and create barriers to seeking fertility treatment. - Psychological Stress: Persistent infections are linked to increased stress and anxiety, further complicating the journey to conception.

Conclusion: These findings highlight the importance of evaluating G. vaginalis in patients with HPV. Future research should

investigate therapies targeting both infections to enhance fertility outcomes.

Keywords: Human Papillomavirus, Gardnerella Vaginalis, Infertility, Female

P-128: Effect of Oral Consumption of Hydroalcoholic Extract of *Linum Usitatissimum* on Morphometric and Histologic Parameters of The Uterus in F1 Female Mice Offspring

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Background: The female reproductive system is important because it plays a fundamental role in fertility, and its proper functioning depends on sex hormones. In the same way, the physiological state of the endometrial layer of the uterus, which is responsible for supporting the fetus, depends on steroid hormones secreted by the ovaries. *Linum usitatissimum* has antioxidant and phytoestrogenic properties due to its special compounds. In this study, we decided to investigate the effect of oral consumption of hydroalcoholic extract of *Linum usitatissimum* on the morphometric and histological parameters of the uterus in first-generation mouse offspring in this study.

Materials and Methods: In this study, 24 female mice were randomly divided into 3 groups: the control (CTL) group, which had no treatment. Treatment groups that take hydroalcoholic extract of flaxseed (FS) with doses of 500 and 1000 mg/kg, respectively. Treatments were started from the first day of pregnancy and until weaning to the mothers and after weaning, the offspring's food was added until 56 days old. At the end of the study, body and uterine weight were measured and stained with hematoxylin and eosin. Also, the thickness of the endometrium and uterus, height of the luminal epithelial cells, and height of the epithelial cells of uterine glands were evaluated.

Results: The results showed that treatment with FS significantly increased the uterine weight and measured parameters compared to the CTL group ($P < 0.05$). While statistical analysis did not show any difference between the two treatment groups in every parameter. The body weight of mice in the CTL group was higher to treatment groups, but it was not significant.

Conclusion: These findings suggest that the natural phytoestrogen, such as FS, is a source of estrogen that could regulate endometrial functions with estrogen receptors and cause improvement in fertility in women.

Keywords: *Linum Usitatissimum*, Uterine, Morphometric, Histologic

P-129: The Therapeutic Potential of *Nigella sativa* in Polycystic Ovary Syndrome : A Systematic Review of Clinical Trials

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Background: Polycystic ovary syndrome (PCOS) is a com-

mon endocrine disorder affecting reproductive-age women, often presenting with oligomenorrhea, hyperandrogenism, and infertility. Conventional treatments can be associated with side effects, leading to growing interest in herbal alternatives such as *Nigella sativa*, traditionally used for hormonal and gynecologic conditions.

Materials and Methods: A systematic review of clinical trials investigating the effects of *Nigella sativa* on women and adolescents with PCOS, or related reproductive conditions, was conducted. Four randomized clinical trials published between 2020 and 2025 were included. Outcomes, including menstrual regularity, hormonal profiles (e.g., LH, testosterone, estradiol), ovarian volume, and clinical symptoms such as hirsutism were assessed. All included studies were double-blind or single-blind and employed either oil-based or capsule formulations of *Nigella sativa*.

Results: *Nigella sativa* supplementation significantly improved menstrual regularity and reduced oligomenorrhea in women with PCOS. Notably, one study demonstrated a reduction in menstrual interval from 86 to 45 days ($P < 0.05$). In adolescents, significant reductions in serum LH and testosterone levels, as well as ovarian volume and hirsutism scores, were reported ($P < 0.001$). Another study found that *Nigella sativa* increased estradiol levels and improved vaginal maturity index in menopausal women, suggesting hormonal modulation. While mild gastrointestinal side effects occurred in a minority of cases, no serious adverse events were reported. One trial on missed abortion cases also suggested *Nigella sativa* may facilitate uterine evacuation.

Conclusion: Current evidence supports the potential efficacy of *Nigella sativa* as a complementary treatment for PCOS-related menstrual and hormonal irregularities. Its favorable safety profile and multiple mechanisms of action highlight its value in integrative gynecologic care. Nonetheless, further large-scale, long-term trials are necessary to establish standardized dosing and clarify its clinical applications.

Keywords: Polycystic Ovary Syndrome, *Nigella Sativa*, Herbal Medicine

P-130: Artificial Intelligence in Predicting Blastocyst Viability and Live Birth: A Systematic Review

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Background: Accurate selection of viable embryos is a critical step in assisted reproductive technology (ART), yet conventional morphology-based assessment methods remain limited in predictive power. Recent advances in artificial intelligence (AI) and image-based analysis offer a promising alternative for improving embryo selection, particularly at the blastocyst stage. This systematic review aims to evaluate the clinical potential and performance of AI models in predicting blastocyst viability, implantation success, and live birth outcomes.

Materials and Methods: A systematic review was conducted on clinical studies (2019–2025) utilizing AI-based models to predict clinical pregnancy or live birth from static or time-lapse blastocyst images. Included studies applied diverse input features—such as embryo morphology, cytoplasmic dynamics, and clinical variables—and employed various machine learning techniques, including neural networks, logistic regression, and

ensemble models, to evaluate predictive performance.

Results: AI models generally outperformed or complemented traditional scoring systems. The control model using Gardner scoring had a pregnancy prediction accuracy of 59.8% (AUC 0.62), while the AI model improved this to 62.7% (AUC 0.68). The ensemble model combining image and clinical data achieved 65.2% accuracy (AUC 0.71). Additionally, cytoplasmic movement analysis using time-lapse imaging and AI resulted in high predictive accuracy (up to 82.6%) for blastocyst development. An AI model for ranking blastocyst embryos demonstrated improved clinical pregnancy prediction over manual grading (AUC 0.6–0.7), although limitations related to microscope type, image quality, and score granularity were identified.

Conclusion: AI-integrated embryo evaluation, particularly with multimodal input, shows promise for optimizing blastocyst selection in ART. While current evidence is encouraging, prospective, multicenter studies are needed to standardize methodologies and validate these models before clinical translation.

Keywords: Artificial Intelligence, Blastocyst, In Vitro Fertilization

P-131: Network Pharmacology to Discover the Mechanisms of Herbal Medicines in Polycystic Ovary Syndrome: A Systematic Review

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Background: Polycystic ovary syndrome (PCOS) is a multifactorial endocrine and metabolic disorder affecting reproductive-aged women. Given the limitations of conventional therapies, herbal medicine has emerged as a promising alternative. Network pharmacology offers a holistic method to elucidate the multi-target mechanisms underlying herbal treatments for PCOS. This systematic review aims to summarize studies that utilize these methods to identify active compounds, molecular targets, and key signaling pathways involved in the herbal treatment of PCOS.

Materials and Methods: A comprehensive literature search was conducted for studies published between 2019 and 2025 using databases such as PubMed, Web of Science, and Google Scholar. Inclusion criteria were original studies applying network pharmacology and/or molecular docking to explore herbal medicines in the context of PCOS. Data were extracted on herb composition, active ingredients, target identification, protein-protein interaction (PPI) networks, pathway enrichment, and validation methods.

Results: Nine eligible studies were included. Frequently investigated herbs and formulas included quercetin, Coptis chinensis, Leonuri Herba, Angelica sinensis–Radix rehmanniae, Yikang decoction, and Jiawei Huanglian–Wendan decoction. Major therapeutic targets included MAPK1, AKT1, IL-6, CXCL8, TP53, and JUN. GO and KEGG enrichment analyses revealed that the PI3K-Akt, MAPK, AGE-RAGE, and TNF signaling pathways are central to the mechanism of action. Molecular docking demonstrated strong binding affinities between active compounds and target proteins. Several studies further validated predictions through animal models or clinical markers, confirming anti-inflammatory, metabolic, and reproductive improvements.

Conclusion: This systematic review demonstrates that network pharmacology and molecular docking provide robust frameworks to unravel the complex mechanisms of herbal medicine in PCOS. The findings support the multi-component, multi-target therapeutic potential of herbal formulations, particularly in regulating inflammation, insulin resistance, and hormonal imbalance.

Keywords: Polycystic Ovary Syndrome, Network Pharmacology, Herbal Medicine

P-132: The Impact of Age on Fertility: A Systematic Review of Reproductive Decline Across the Lifespan

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Background: Age is a critical factor influencing human fertility, yet its effects differ notably between genders. Female reproductive potential declines more rapidly and predictably than male fertility, impacting natural conception and assisted reproductive outcomes.

Materials and Methods: To systematically review and synthesize current evidence on how increasing age affects fertility, including ovarian/testicular reserve, gamete quality, and assisted reproductive technologies (ART) success rates. A systematic search was conducted in PubMed, Embase, Scopus, and Web of Science for human studies published from January 2000 to March 2025. Studies were included if they quantitatively assessed fertility outcomes—such as anti-Müllerian hormone (AMH) levels, antral follicle count, semen parameters, or ART success across defined age groups. Two reviewers independently screened and extracted data following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results: Of 5,213 records screened, 67 studies met the inclusion criteria. In women, fertility showed a significant decline after age 35, with lower AMH, reduced follicle count, and decreased oocyte quality. Male fertility decline was more gradual, with diminished semen volume, motility, and DNA integrity noticeable after age 40. ART outcomes were inversely correlated with age, especially in women over 38. Some studies also reported compounded negative effects when both partners were of advanced age.

Conclusion: Age exerts a measurable and multifaceted impact on fertility. While male fertility shows a slower decline, female reproductive aging is more abrupt and biologically constrained. These findings emphasize the importance of timely reproductive planning and provide valuable insight for clinical counseling. Future longitudinal studies are needed to distinguish the effects of aging from those of modifiable lifestyle or environmental exposures.

Keywords: Fertility, Maternal Age, Gamete Quality, Ovarian Reserve, ART

P-133: The Association of SLE Duration with Childbearing in Women with Systemic Lupus Erythematosus

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Background: Systemic lupus erythematosus (SLE) is a concern for women's childbearing. This study aimed to examine the impact of SLE duration on women's childbearing.

Materials and Methods: This study was conducted on 429 women of reproductive age (15–49 years) with SLE. Research was conducted from January 21, 2023, to March 20, 2024, in the rheumatology clinic and the Iranian Lupus Association of Tehran, Iran. Data was randomly collected through an online questionnaire. The data collection instruments included the researcher making questionnaires (SLE duration: less than 1, 1-5, 5-10, more than 10 years; the category of pregnancies, births, and children's numbers (0, 1-2, 3-4, more than 4) before and after contracting SLE). The collected data were entered into SPSS software version 27 and analyzed using Kendall's Tau test at a significant level of $P < 0.01$.

Results: The findings revealed a significant relationship between the SLE duration with other diseases associated with SLE ($R: 0.18$, $P: < .001$, $CI95\%: 0.08$ to 0.27), the number of pregnancies ($R: 0.296$, $P: < .001$, $CI95\%: 0.21$ to 0.37), the number of birth ($R: 0.234$, $P: < .001$, $CI95\%: 0.15$ to 0.31), and the number of children ($R: 0.203$, $P: < .001$, $CI95\%: 0.12$ to 0.28) after contracting SLE.

Conclusion: According to the finding of study, despite the increase in diseases associated with SLE as the duration of SLE has prolonged, the number of pregnancies, births, and children of women with SLE has increased, perhaps one of the most important reasons for this is the suitable care and monitoring programs of the rheumatology clinic and Iranian Lupus Association of Tehran, Iran.

Keywords: Systemic Lupus Erythematosus, Women, Childbearing

P-134: Assessment of Anthropometric Indices in Women with Polycystic Ovary Syndrome: A Cross-Sectional Study at Fatemeh Zahra Specialized Infertility Center in Babol, 2018–2023

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Background: Polycystic ovary syndrome (PCOS) is recognized as one of the leading causes of infertility in women. Given the easy accessibility, low cost, and clinical relevance of anthropometric indices, this study aimed to evaluate these indices in patients with PCOS.

Materials and Methods: This cross-sectional study, part of a retrospective cohort, included 182 women referred to the

Fatemeh Zahra Infertility Center in Babol, Iran, between 2018 and 2023 (Solar Hijri calendar: 1397–1402). Anthropometric parameters such as height, weight, waist circumference, hip circumference, arm circumference, wrist circumference, neck circumference, and body mass index (BMI) were measured in women diagnosed with PCOS.

Results: Among the 182 women with PCOS (mean age: 27.53 ± 5.63 years), anthropometric indices, including weight, waist circumference, hip circumference, and BMI, were significantly higher in the high school-educated group compared to other educational levels ($P < 0.05$). No significant associations were observed between anthropometric indices and occupation, medication history, or comorbidities ($p > 0.05$), except for greater height in individuals with cardiovascular disease ($P = 0.044$). Laboratory findings revealed a positive correlation between arm circumference and abnormal LH levels, as well as between abnormal FBS levels and weight, hip circumference, wrist circumference, and BMI ($P < 0.05$). Additionally, abnormal prolactin levels were associated with increased hip circumference, arm circumference, and wrist circumference ($P < 0.05$).

Conclusion: The findings suggest that anthropometric indices can serve as complementary tools for evaluating and managing infertile patients with PCOS. These low-cost indices demonstrate significant potential for integration into diagnostic and therapeutic protocols, enhancing clinical decision-making.

Keywords: Anthropometry, Infertility, Polycystic Ovary Syndrome

P-135: Comparing Body Image in Women with and without Polycystic Ovarian Syndrome

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Background: Body image is how a person perceives their body, including appearance, size, health, and function. It also covers feelings, thoughts, and actions regarding the body and appearance. Some studies have shown a more negative body image in women with PCOS compared to healthy women. Still, some cross-sectional studies have shown that body image does not differ between PCOS women and healthy women after adjustment for body mass index (BMI). The purpose of this study was to compare body image in women with and without PCOS.

Materials and Methods: This case-control study included 138 women with PCOS diagnosed by the Rotterdam criteria and 160 age- and BMI-matched controls. Participants who were 18–40 years old and literate were included. Study exclusion criteria were pregnancy, lactation, mental illness, use of special diets, or exercise in the previous 6 months. Body image was assessed with Body Shape Questionnaire (BSQ). It included 34 questions about body shape, weight concerns, and affective, cognitive, and behavioral aspects. Participants rated each item on a six-point Likert scale. The lowest score is 34, and the highest score is 204. This scale is used to predict an individual's body image satisfaction. Scores under 80 are defined as no dissatisfaction, 80 to 110 as mild dissatisfaction, 111 to 140 as moderate dissatisfaction, and more than 140 as severe dissatisfaction.

Results: The mean BMI and age in the PCOS group were (30.1 ± 3.62 kg/m², 29.5 ± 4.3 years) and in the controls (29.5 ± 3.5

kg/m², 28.5 ± 5.2 years) (P>0.05). Women with PCOS had significantly higher mean BSQ scores (129.3 ± 21.2) than those without PCOS (84.5 ± 15.6) (P<0.001). In multivariable regression models adjusted for age, BMI, pregnancy history, infertility history, income, and employment, BSQ scores were statistically significantly higher in women with PCOS compared with controls. In both groups, higher BMI was associated with greater body dissatisfaction.

Conclusion: Our data suggest that polycystic ovary syndrome has a negative impact on body image.

Keywords: Polycystic Ovary Syndrome, Body Image, Body Dissatisfaction

P-136: The Role of The Final Oocyte Triggering Method in the Double Ovarian Stimulation Protocol: A Retrospective Cohort Study

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Background: This study aimed to investigate the relationship between the type of final oocyte trigger used in the follicular and luteal stimulation phases and the number of metaphase II (MII) oocytes in each phase during double ovarian stimulation (DouStim) cycles.

Materials and Methods: This retrospective cohort study examined the ovarian stimulation cycles of patients with poor ovarian response diagnosis who underwent the DuoStim protocol at the Royan Institute between 2021 and 2023. Data was collected from the Royan Institute's database system. In total, the ovarian stimulation outcomes of 411 patients were analyzed. Out of these, 189 patients underwent DuoStim cycles using two gonadotropin-releasing hormone (GnRH) antagonists (Anta-Anta), while 222 patients used a combination of a GnRH antagonist and Medroxyprogesterone (Anta-Progestin) approaches. Final oocyte triggering in these treatment cycles, during both the follicular and luteal phases, was performed based on the physician's discretion using one of three methods: GnRH-agonist alone, human chorionic gonadotropin (hCG) alone, or a combination of both (dual trigger).

Results: The analysis indicated that there were no statistically significant differences between the two groups regarding women's age, ovarian reserve tests, or the causes of infertility. In the overall population, the type of final oocyte trigger was significantly associated with the number of MII oocytes during the luteal phase (P=0.024). Specifically, the dual trigger method in this phase resulted in a higher rate of mature oocytes. Further investigation revealed a significant relationship between the type of trigger in the luteal phase and the number of MII oocytes when employing the Anta-Anta approach (P=0.009); however, this relationship was not observed with the Anta-Progestin approach (P=0.700).

Conclusion: The dual trigger method in the luteal phase stimu-

lation is associated with more mature oocytes. However, further prospective studies with larger sample sizes are needed to confirm these findings.

Keywords: Doustim Protocol, Mature Oocyte, Dual Trigger, Medroxyprogesterone, GnRH-Antagonist

P-137: The Effect of Metformin on Oxidative Stress Markers in Women with Polycystic Ovary Syndrome Undergoing Intracytoplasmic Sperm Injection

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Background: Polycystic ovary syndrome (PCOS) is characterized by insulin resistance and hyperandrogenism, which contribute to increased production of reactive oxygen species (ROS) and reduced activity of antioxidant enzymes. Metformin, a common drug in the treatment of PCOS, not only improves insulin sensitivity and corrects hormonal imbalances but may also reduce oxidative stress. The aim was to investigate the effects of metformin on oxidative stress levels and antioxidant enzyme activity in the serum and follicular fluid of women with PCOS.

Materials and Methods: Forty women with PCOS were randomly assigned to receive either metformin (1500 mg) or a placebo (25 mg ORS solution) for 8 weeks, starting two months before ovulation and continuing until oocyte retrieval. Serum and follicular fluid levels of malondialdehyde (MDA), total antioxidant capacity (TAC), and glutathione peroxidase/glutathione reductase (GPX/GRD) were measured using ELISA. Data were analyzed using the Independent T-Test, and the difference between means was considered significant at the P<0.05 level.

Results: The mean serum MDA levels (P=0.03) and follicular fluid mean MDA levels (P=0.001) decreased significantly between the placebo and metformin groups. The mean serum TAC levels increased significantly between the placebo and metformin groups (P<0.001). There was no significant difference in follicular fluid mean TAC levels between the placebo and metformin groups (P=0.276). There was no significant difference in the mean levels of GPX and GR in serum and follicular fluid between the placebo and metformin groups (P > 0.05).

Conclusion: Our results showed that Metformin reduced oxidative stress in women with PCOS by decreasing MDA levels and increasing serum TAC. However, it had no significant effect on GPX, GR, or TAC levels in follicular fluid, suggesting that its antioxidant effects are primarily systemic rather than localized within the follicular environment.

Keywords: PCOS, MDA, TAC, GPX, Oocyte Quality

P-138: Empagliflozin Improves Serum and Follicular Fluid Reproductive Hormone Profiles in Women with Polycystic Ovary Syndrome Undergoing Intracytoplasmic Sperm Injection

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Background: Polycystic ovary syndrome (PCOS) is an endocrine disorder marked by insulin resistance, hyperglycemia, and reproductive dysfunction. Empagliflozin (EMPA), a sodium-glucose cotransporter 2 (SGLT2) inhibitor, reduces blood glucose in type 2 diabetes and may be beneficial for PCOS due to shared metabolic features. This study investigated the effects of empagliflozin on serum and follicular fluid levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T), and estradiol (E2) in women with PCOS.

Materials and Methods: Forty women with PCOS were randomly divided into two groups. Empagliflozin (25 mg) and placebo (25 mg ORS solution) were both administered for 8 weeks. Treatment was started two months before the oocyte cycle and continued until the day of oocyte retrieval. Finally, serum and follicular fluid LH, FSH, testosterone, and estradiol levels were measured by ELISA (Enzyme-Linked Immunosorbent Assay). Data were analyzed using the Independent T-Test, and the difference between means was considered significant at the $P < 0.05$ level.

Results: After two months, the empagliflozin group showed a significant reduction in serum and follicular fluid LH levels compared to the placebo group ($P < 0.001$). No significant differences were found in FSH levels in either serum ($P = 0.27$) or follicular fluid ($P = 0.07$). While serum estradiol levels were similar between groups ($P = 0.8$), follicular fluid estradiol was significantly lower in the empagliflozin group ($P < 0.001$). Testosterone levels did not differ significantly in serum ($P = 0.954$) or follicular fluid ($P = 0.910$).

Conclusion: The results indicated that empagliflozin reduced LH and follicular fluid estradiol levels in women with PCOS, suggesting its potential to improve hormonal imbalances. Further research is needed to confirm its long-term efficacy and safety.

Keywords: PCOS, Empagliflozin, LH, Testosterone, Estradiol

P-139: The Association of The First Coitus Age with STD History in People Contracted with HPV

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Background: Human Papillomavirus (HPV) is the most common sexually transmitted disease. The age of first coitus in HPV people may play a role in inducing STD. This study aimed to assess the relation of first coitus age with STD history in people contracted with HPV.

Materials and Methods: This study was conducted on 429 people (220 women and 209 men) with HPV from Sep 15, 2023, to Apr 30, 2024, in the Hospitals of Tabriz, Iran. Data was randomly collected through a questionnaire. The data collection instruments included the researcher making question-

naires (STD history: yes, no). The collected data were entered into SPSS 27 software and analyzed using an independent t-test at a significant level of $P < 0.01$.

Results: Mean (Standard deviation) of first coitus age in females was 21.06 (5.54) (min-max:12-45) and males was 23.15(5.27) (min-max:15-46). Research showed a significant association of first coitus age with STD history (t : 17.77, df : 2, p : 0.009). According to the hedges correlation value (0.449, CI 95%: 0.16 to 0.73) their correlation had a medium effect.

Conclusion: The findings revealed a medium effect of first coitus age on STD history in people with HPV, so a lower first coitus age of females and males was associated with more STDs in HPV patients.

Keywords: Sexually Transmitted Disease, Human Papillomavirus, Coitus

P-140: The Association of Genital Laser Epilation with STD History in People Contracted with HPV

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Background: Human Papillomavirus (HPV) is the most common sexually transmitted disease that be able to be transmitted through cosmetic procedures. This study aimed to assess the relation of genital laser epilation with STD history in people contracted with HPV.

Materials and Methods: This study was conducted on 429 people (220 women and 209 men) with HPV from Sep 15, 2023, to Apr 30, 2024, in the Hospitals of Tabriz, Iran. Data was randomly collected through a questionnaire. The data collection instruments included the researcher making questionnaires (Genital Laser Epilation: no, laser, epilation, both; STD history: yes, no). The collected data were entered into SPSS 27 software and analyzed using Pearson's and chi-square at a significant level of $P < 0.01$.

Results: In this study, 33.6% females and 4.4% males used the genital laser. Also, 21.2% females and 3.8% males had STDs. The findings revealed a significant relationship between genital laser epilation with STD history (χ^2 : 17.77, df : 2, p : 0.009). According to Cramer's correlation value (v : 0.148), their correlation was moderate.

Conclusion: According to the study findings, despite the relation of genital laser epilation with STD history in people contracted with HPV, their associations were moderate. Maybe other reasons under it can exaggerate the STDs of people who contracted HPV.

Keywords: Sexually Transmitted Disease, Human Papillomavirus, Laser, Epilation

P-141: Improved Ovarian Histological Indices in Polycystic Ovary Syndrome Treated with Exenatide

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Background: Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder that can cause infertility. The polycystic ovary has six to eight times more pre-antral and small antral follicles that are arrested at a size of 2-9 mm, and dominant follicles were not formed by excess androgens.

Materials and Methods: Twenty-eight adult female Wistar rats were divided into four groups. The normal group did not receive any drug. The PCOS + vehicle (Veh) group received estradiol valerate to induce PCOS, then was divided into PCOS+ Exe 50 and PCOS+ Exe 100 groups and treated with 50 or 100 µg/kg doses of exenatide, respectively.

Results: Our results showed that the size of the follicles in different groups did not differ. In the treatment groups at doses of 50 and 100 µg/kg, the number of ovarian cysts was lower than in the PCO group. In the group receiving exenatide, the thickness of the theca layer was reduced by dose of 50 compared to the PCO group. Also, the thickness of the granulosa layer was more developed in the groups treated with exenatide 50. In the treated groups, especially with the dose of 50 µg/kg exenatide, the number of corpora lutea was more than in the PCO group.

Conclusion: Exenatide, a glucagon-like peptide, had useful effects on ovarian histological indices.

Keywords: Polycystic Ovarian Syndrome, Exenatide, Cystic Follicles

P-142: Morphometric Analysis of The Peri-Implantation Endometrium of Infertile Women with Hydrosalpinx Before and After Salpingectomy Using Hematoxylin and Eosin Biopsy Samples

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Background: Hydrosalpinx is a condition in which fluid accumulates in the fallopian tubes, adversely affecting reproductive outcomes and the structure of the endometrium. This study examines the histological changes in the endometrium associated with hydrosalpinx, both before and after salpingectomy, and compares these findings to those from fertile individuals

Materials and Methods: A total of thirty subjects, including 10 patients with unilateral hydrosalpinx undergoing salpingectomy

and 20 healthy fertile women with successful pregnancies, were studied. All participants had normal hormonal profiles, body mass index, and regular menstrual cycles. Endometrial biopsies were collected during the mid-secretory phase before salpingectomy and again four months post-surgery. Morphometric analysis was performed using the high-resolution histopathological microscope to quantify surface and glandular epithelial cell height, average glandular diameter and glandular luminal diameter, glandular stromal fraction, and glandular density. These variables were compared between hydrosalpinx and controls, and before and after salpingectomy. The Wilcoxon Rank test was used for data analysis of before and after salpingectomy, and P<0.05 was considered significant.

Results: Before the salpingectomy, there were significant decreases in the height of both surface and glandular epithelium, as well as in average glandular and luminal diameter, and glandular density when compared to the control group (P<0.05). Following the salpingectomy, significant increases were observed in the height of surface and glandular epithelium, the average glandular diameter, and the luminal diameter of glands (P<0.05).

Conclusion: Surgical removal of hydrosalpinx is associated with improved endometrial structure, highlighting its importance in managing hydrosalpinx patients during IVF cycles. Prompt intervention is vital for enhancing reproductive success.

Keywords: Hydrosalpinx, Peri-Implantation Endometrium, Salpingectomy, Morphometry, Light Microscopy

Genetics

P-143: A Compound Heterozygous Variant in the SOX30 Gene Could Cause Idiopathic Male Infertility

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Background: Male infertility is a growing issue affecting approximately 50 million couples worldwide, often with unknown underlying causes. Spermatogenesis is the complex process during testicular development that transforms diploid spermatogonial stem cells into haploid spermatozoa capable of fertilizing oocytes. Recent studies suggest that the *SOX30* gene is involved in this process. The *SOX* (Sry-related High Mobility Group (HMG) box) gene family includes transcription factors critical for sex determination, neuronal development, and stem cell regulation. *SOX30*, the sole member of *SOX* group H, is relatively divergent, with an HMG domain that is only 46% identical to the consensus sequence of the *SOX*-HMG box.

Materials and Methods: We assessed a patient with male infertility caused by asthenoteratozoospermia. Through whole-exome sequencing (WES) and Sanger sequencing, we identified a compound heterozygous variant in the *SOX30* gene. To inves-

tigate the molecular effects of these variants, we used Project HOPE to analyze the impact of missense mutations on protein structure and I-Mutant to predict changes in protein stability.

Results: WES revealed a compound heterozygous variant in the *SOX30* gene (c.163T>C and c.830G>A) in a patient with asthenoteratozoospermia. Prediction databases such as Mutation-Taster, STIF, Project HOPE, and I-Mutant suggest these missense mutations may affect the protein's structure and stability, potentially impairing its role in spermatogenesis. The patient inherited one mutated allele from each parent.

Conclusion: Our findings show compound heterozygous variants in the *SOX30* gene in a patient with asthenoteratozoospermia. Computational predictions indicate that these mutations may destabilize the SOX30 protein, impairing its function in spermatogenesis. This study provides new evidence supporting *SOX30* as a candidate gene linked to male infertility.

Keywords: Idiopathic Male Infertility, Whole-Exome Sequencing, Computational Analysis, SOX30

P-144: A Missense Variant in The STIM1 Gene and Its Correlation with Unexplained Male Infertility

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Background: The World Health Organization defines infertility as the inability to conceive after one year of unprotected sexual intercourse, affecting approximately 50 million couples worldwide equally among men and women. Male infertility is often linked to conditions like Klinefelter syndrome and Y Chromosome Microdeletions (YCMDs), with 60-70% of cases having unknown causes. Calcium release in sperm is paired with extracellular calcium entry through specialized channels, particularly involving the store-operated calcium entry (SOCE) pathway. This pathway relies on two key proteins, ORAI and STIM, essential for sperm function, especially in regulating hypermotility and the acrosome reaction

Materials and Methods: We assessed a patient with unexplained male infertility, whose brother also has a similar issue. Additionally, their parents are first cousins. Using whole-exome sequencing (WES), we analyzed the data through bioinformatics databases and confirmed the findings with Sanger sequencing. To explore the molecular effects of these variants, we used Project HOPE to evaluate how missense mutations affect protein structure and properties, along with mCSM to analyze changes in stability.

Results: Whole-exome sequencing identified a homozygous variant in the *STIM1* gene in a patient and his brother with unexplained male infertility. Bioinformatics analysis predicted that this missense mutation may disrupt STIM1 protein struc-

ture and stability, impairing calcium signaling, sperm motility, and the acrosome reaction.

Conclusion: Through WES, we identified a homozygous variant in the *STIM1* gene in a patient with unexplained male infertility. This missense mutation appears to alter STIM1 protein structure and disrupt calcium homeostasis in sperm, suggesting a new genetic mechanism for male infertility.

Keywords: Unexplained Male Infertility, Whole-Exome Sequencing, Bioinformatics Analysis, STIM1

P-145: Polymorphisms in The TEX15 Gene and Their Association with Male Infertility: A Systematic Review

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Background: The *TEX15* (Testis-expressed 15) gene functions as a meiosis-specific gene that plays an essential role in DNA double-strand break repair processes during spermatogenesis. Research shows that *TEX15* gene polymorphisms lead to male infertility, especially in cases of non-obstructive azoospermia (NOA) and oligozoospermia. Recent genomic studies have demonstrated that this gene can be used as a clinical factor in spermatogenic failure detection.

Materials and Methods: The systematic review followed PRISMA guidelines. The research team conducted database searches through PubMed, Scopus, and Google Scholar to retrieve articles from 2020 to 2025. The research included human studies that investigated the relationship between *TEX15* gene polymorphisms and male infertility. The research included case-control studies together with genome-wide association studies (GWAS) and next-generation sequencing (NGS) analyses. The quality assessment using the Newcastle-Ottawa Scale resulted in 11 studies meeting the inclusion criteria.

Results: The *TEX15* gene contains multiple single nucleotide polymorphisms (SNPs) which show consistent links to male infertility across different populations. The rs323344 and rs61732458 polymorphisms showed a significant connection to NOA and oligozoospermia in both Iranian and Vietnamese population studies. The study conducted by used exome sequencing to validate the extensive genetic diversity of *TEX15* variants that affect spermatogenic failure in men. A genetic study found *TEX15* to be one of the essential genes that contribute to Spermatogenic Failure type 25 (SPGF25).

Conclusion: The *TEX15* gene contains polymorphisms that directly link to different forms of male infertility, especially NOA. The rs323344 and rs61732458 markers show consistent results across different populations yet researchers need to study ethnic-specific variants together with gene-environment interactions. The research evidence supports the implementation of *TEX15* polymorphism testing as a diagnostic tool for idiopathic male infertility.

Keywords: *TEX15*, Male Infertility, Non-obstructive Azoospermia, Genetic Polymorphism, Single Nucleotide Polymorphism

P-146: Regulatory RNA Profiles Associated with TEX15 and Their Role in Spermatogenic Disorders Among Infertile Men: A Systematic Review

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Background: The *TEX15* gene functions as a crucial factor for homologous recombination and chromosome synapsis during meiosis and has been identified as a major cause of non-obstructive azoospermia (NOA). Research findings demonstrate that regulatory RNAs including miRNAs, piRNAs, and lncRNAs play essential roles in controlling *TEX15* expression and spermatogenic pathways.

Materials and Methods: The research followed PRISMA guidelines for its systematic review. The search included PubMed, Scopus, and Web of Science databases for articles from January 2020 to May 2025 using the keywords "TEX15", "regulatory RNAs", "spermatogenesis", and "male infertility". The inclusion criteria consisted of original research and systematic reviews that established connections between regulatory RNAs and *TEX15* function and spermatogenic defects in human male infertility. Thirteen studies met eligibility.

Results: Multiple studies confirm *TEX15*'s expression in spermatogonia and early spermatocytes, with homozygous mutations causing meiotic arrest. The testicular tissue of subfertile men shows elevated levels of miR-23a-3p and miR-23b-3p which target *TEX15* and other genes that could interfere with spermatogenesis. The testicular piRNA dysregulation involving *TEX15* was also reported in NOA patients. The *TEX15* mutations lead to spermatogenic arrest and defective recombination because of disruptions in regulatory regions.

Conclusion: This review consolidates evidence that regulatory RNAs are integral to *TEX15*-mediated spermatogenesis. Aberrant expression or epigenetic modulation of these RNAs may serve as both biomarkers and therapeutic targets in male infertility diagnostics. The miR-23 family members together with specific piRNA clusters control meiotic progression through *TEX15* post-transcriptional regulation which leads to DSB repair errors. The *TEX15* loci undergo chromatin remodeling through lncRNA mechanisms which establishes a functional connection between non-coding RNA structure and meiotic gene regulation. Future multi-omics approaches integrating transcriptomics, epigenomics, and chromatin conformation analysis are required to unravel complex RNA-gene interactions influencing *TEX15*.

Keywords: *TEX15* gene, Regulatory RNAs, Spermatogenesis, piRNA Dysregulation, Male Infertility Biomarkers

P-147: Evaluating of *VEGF* Gene Expression in Women with Secondary Infertility Isthmocele Grade 3 Compared to Fertile Women

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Background: Isthmocele, also referred to as a uterine niche or diverticulum, is a myometrial scar defect that develops at the site of a previous cesarean section, typically forming a pouch-like structure on the anterior wall of the uterine isthmus. This iatrogenic defect may impair endometrial integrity and has been implicated in secondary infertility. Vascular endothelial growth factor (VEGF) is a potent angiogenic factor that plays a critical role in various physiological and pathological processes. Proper angiogenesis is essential for endometrial development and differentiation, which are necessary for successful implantation. Alterations in VEGF expression have been associated with reproductive failures such as recurrent implantation failure and miscarriage. Given the importance of VEGF in endometrial function, it is hypothesized that disrupted VEGF expression may contribute to embryo implantation failure in women with isthmocele.

Materials and Methods: In this case-control study, endometrial tissue samples were collected between day 17-21 of the menstrual cycle (WOI) from 10 infertile women with isthmocele grade 3 (case group) and 10 healthy fertile women (control group). *VEGF* gene expression was assessed using quantitative polymerase chain reaction (Q-PCR).

Results: Q-PCR data analysis identified significantly higher expression of VEGF in women with isthmocele (case group) compared with fertile women (control group) ($P \leq 0.05$).

Conclusion: Our findings demonstrate that VEGF gene expression is significantly upregulated in women with grade 3 isthmocele compared to fertile controls. Therefore, this abnormal upregulation may disrupt normal angiogenesis and impair endometrial receptivity, potentially leading to implantation failure and secondary infertility.

Keywords: Isthmocele, Implantation Failure, Secondary Infertility, VEGF

P-148: Identification of Genetics Variants Associated with Sporadic Idiopathic Primary Ovarian Insufficiency

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Background: Premature ovarian insufficiency (POI) is a heterogeneous disorder characterized by the loss of ovarian function before the age of 40, affecting approximately 1-4% of women worldwide. While Known genetic causes account for 20-30% of POI cases, the etiology in many sporadic non-syndromic cases remains unclear. The aim of this study was to investigate the genetic basis of sporadic POI using whole exome sequencing (WES), to identify candidate variants that may contribute to

the disease pathogenesis.

Materials and Methods: WES was performed on DNA samples from three unrelated women diagnosed with sporadic idiopathic POI. The ACMG guideline was considered for variant classification. Bioinformatic analysis and interpretation of candidate variants were performed using comprehensive genomic and transcriptomic databases including Franklin, Varsome, Malacards, Genecards, Gtexportal, Proteatlas and Mobi-Details. Polymerase chain reaction (PCR) amplification was conducted for candidate variants and Sanger sequencing was used to validate the detected potentially variants in proband and available relatives.

Results: In total nine candidate genes were identified. Three variants were classified as pathogenic/likely pathogenic, and six variants were uncertain significance (VUS) and one of them was a novel candidate gene, that has not been reported in POI so far. Two of genes *LARS2* and *BRCA2* was previously reported in association with POI. This study also identified six novel variants in *CPEB1*, *DDBI*, *NOTCH1*, *CYP11B1*, *EIF2B5* and *HMMR*. These genes were considered candidates as they have known function during processes of meiosis, DNA repair, cell cycle control and mitochondrial function.

Conclusion: This study supports the contribution of potentially pathogenic/likely pathogenic variants to the genetic architecture of sporadic idiopathic POI. Identification of novel genes and unreported variants expands our understanding of POI pathogenesis as an oligogenic disease and underscores the utility of WES as a diagnostic tool in uncovering hidden genetic causes of female infertility.

Keywords: Primary Ovarian Insufficiency, Whole-Exome Sequencing, Sporadic, Genetic Variants

P-149: Epigenetic Modifications and Gene Expression of *GDF9*, *BMP15*, and *IL-6* in Cumulus Cells of Endometriosis Patients: Implications for Oocyte Competence

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Background: Endometriosis is a gynecological and epigenetic disorder. Since endometriosis patients have poor ovarian reserve and oocyte developmental competence, non-invasive assessments such as Cumulus cells (CCs) should be used to determine oocyte quality. *GDF9*, *BMP15*, and *IL-6* have a critical impact on oocyte maturation. Therefore, this study aims to evaluate epigenetic alterations and expression of candidate genes in CCs of women diagnosed with endometriosis compared to healthy controls.

Materials and Methods: CC samples were collected from the

patients (stage III or IV) and the control groups according to the inclusion and non-inclusion criteria. RNA extraction, cDNA synthesis, and qRT-PCR were performed for case and control groups (n=30). Epigenetic modifications were also evaluated using chromatin immunoprecipitation and qRT-PCR for pooled CCs samples (n=24).

Results: In this study, H3K9ac levels of *BMP15* and *GDF9* were decreased, and *IL-6* was increased in women with endometriosis compared to controls, which was significant for *IL-6* (P=0.0002). In contrast, H3K9me2 and DNA methylation showed a significant increase in *BMP15* (P<0.0001 and P=0.0002, respectively) and *GDF9* (P=0.0029 and P=0.0348, respectively) in the patients compared to the control group. According to this study, H3K9 hypomethylation and a significant decrease in DNA methylation of *IL-6* (P=0.0098) were observed in the endometriosis compared to the control group. Clinical outcomes analysis showed a significant decrease in the number of MII oocytes (P=0.0205), and the number of retrieved oocytes tended to be lower (P=0.0553) in the case compared to the control group.

Conclusion: It seems that epigenetic modifications and expression changes of *GDF9*, *BMP15*, and *IL-6* in CCs of endometriosis women can cause a decrease in oocyte quality. Changes in the expression of candidate genes can be associated with disruption of folliculogenesis and oocyte maturation, with a decrease in the number of MII oocytes in the patients, which was also confirmed by the clinical data of this study.

Keywords: Endometriosis, Cumulus Cells, Oocyte Maturation Genes, Oocyte Quality, Epigenetic Alterations

P-150 Evaluation of NF-κB Gene Expression in the Endometrium of Women with Isthmocele during The Window of Implantation

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Background: Isthmocele, also known as a cesarean scar defect, refers to a niche-like pouch in the anterior uterine wall at the site of a previous cesarean section. The presence of a niche at the site of a cesarean scar can create an unfavorable environment disrupting the normal function of the endometrium and potentially leading to impaired fertility. In this context, one of the key molecular regulators of inflammation is the nuclear factor kappa B (NF-κB), a transcription factor involved in the expression of numerous pro-inflammatory genes. Dysregulation of the NF-κB gene may impair endometrial receptivity through chronic inflammation and immune imbalance, and may potentially lead to implantation failure in secondary infertility associated with Isthmocele.

Materials and Methods: In this case-control study, 10 infertile women with isthmocele grade 3 (case group) and 10 fertile women (control group) participated. NF-κB mRNA expression was assessed using real-time PCR, and results were analyzed to compare the two groups.

Results: The results indicate a significant increase in NF-κB

gene expression in the Isthmocele group compared to the control group ($P \leq 0.05$).

Conclusion: A certain degree of inflammation is essential for successful implantation and pregnancy. However, excessive or dysregulated inflammatory responses potentially mediated by pathways such as NF- κ B may disrupt endometrial receptivity and negatively impact implantation outcomes, thereby contributing to secondary infertility.

Keywords: NF- κ B, Isthmocele, Implantation

P-1:151 Cumulus Cell Transcriptome Signatures as Predictive Biomarkers in ART: A Cross-Sectional Prospective Study of Molecular Determinants for Embryo Competence and Pregnancy Outcomes

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Background: Conventional morphological assessment for embryo selection in assisted reproductive technology (ART) has limited predictive value. Cumulus cells provide potential non-invasive biomarkers for oocyte quality. This study examined whether CALM1, PSMD6, and AK124742 could predict pregnancy outcomes, particularly in polycystic ovary syndrome (PCOS) patients.

Materials and Methods: This cross-sectional prospective study included 66 patients (33 PCOS, 33 controls) undergoing IVF/ICSI treatment. Gene expression in cumulus cells was analyzed using qRT-PCR with *GAPDH* as reference. Pregnancy outcomes were tracked through β -hCG testing and ultrasound confirmation.

Results: All three genes showed elevated expression in pregnant versus non-pregnant groups, with *PSMD6* ($P < 0.001$) and *AK124742* ($P < 0.05$) reaching statistical significance. PCOS patients showed significantly higher *CALM1* and *AK124742* expression ($P = 0.003$, $P < 0.001$) and lower *PSMD6* expression ($P = 0.002$) compared to controls, independent of pregnancy status. Age-adjusted analysis revealed significantly elevated *CALM1* in pregnant patients ($P < 0.05$). PCOS patients produced more oocytes (14.15 vs. 9.03, $P = 0.005$) without corresponding higher pregnancy rates. IVF achieved higher success rates than ICSI (85.7% vs. 43.3%, $P = 0.007$). Sperm morphology correlated significantly with fertilization rates ($r^2 = 0.337$, $P < 0.001$).

Conclusion: While all three genes showed potential as biomarkers for embryo competence, their expression patterns were significantly altered in PCOS patients. PCOS influenced gene expression more strongly than pregnancy outcome alone, suggesting ovarian pathophysiology significantly impacts cumulus cell molecular signatures. These findings emphasize the importance of considering underlying ovarian health when developing genetic predictors of embryo viability, potentially enabling more personalized fertility treatment approaches.

Keywords: Assisted Reproductive Techniques, Gene Expression, Cumulus Cells, Embryo Selection, PCOS

P-152: Synergy of Age and Endometriosis in Infertility: The Role of PTGS2, BMP15, and IL-6 Expression

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Background: Endometriosis and aging are both important factors in infertility of women, which can disrupt the ovulation process. With increasing age, significant genomic changes occur in the Cumulus cells (CCs) and follicular fluid (FF), which are critical for oocyte maturation. Therefore, reproductive aging in endometriosis patients can increase the risk of infertility. *BMP15*, *IL-6*, and *PTGS2* are key genes involved in oocyte maturation. This study aims to investigate the association between aging and the expression levels of *BMP15*, *IL-6*, and *PTGS2* in the CCs and FF of endometriosis patients.

Materials and Methods: In our previous study, we observed a significant decrease in *BMP15* and *PTGS2* expression and a significant increase in *IL-6* expression in the FF and CCs of the endometriosis group ($n = 30$) compared to the control group ($n = 30$), using qRT-PCR ($P < 0.0001$). In this study, Pearson (parametric data) and Spearman (non-parametric data) correlation tests were applied to evaluate the relationship between gene expression levels and age in endometriosis patients. The significance level was considered to be $P \leq 0.05$.

Results: The results indicated that with increasing age, in the endometriosis group, *BMP15* expression in FF decreased significantly ($r = -0.3749$; $P = 0.0412$). Similarly, *IL-6* mRNA levels in CCs showed a significant inverse correlation with age in endometriosis patients ($r = -0.4361$; $P = 0.0160$). *PTGS2* expression in both FF and CCs was also inversely correlated with age ($r = -0.4176$; $P = 0.0217$ and $r = -0.4807$; $P = 0.0072$, respectively). Furthermore, analysis using the STRING database revealed interactions among the candidate genes.

Conclusion: Alterations in the gene expression of *BMP15*, *IL-6*, and *PTGS2* may impair CCs expansion and oocyte developmental competence. Consequently, aging in endometriosis patients could contribute to impaired oocyte maturation and ovulation defects through transcriptional dysregulation. Nevertheless, to elucidate the link between oocyte quality and age in endometriosis, comprehensive transcriptomic profiling of FF and CCs is warranted.

Keywords: Endometriosis, Aging, *BMP15*, *IL-6*, *PTGS2*

P-153: Gene Expression Patterns of IL-33, IL-33 Receptor and IL-37 in the endometrium of Women with Endometriosis

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Background: Endometriosis is a chronic inflammatory disease marked by the presence of endometrial-like tissue outside the uterine. While its exact underlying mechanisms are still not fully understood, disruptions in immune functions are believed to contribute to endometriosis. Cytokines as one of key players in immune and inflammatory responses consist of different families, including interleukin-1 (IL-1) family. Among IL-1 family, IL-33 is known for its pro-inflammatory activity via interaction with its receptor ST2, whereas IL-37 acts as a natural suppressor of inflammation. This study aimed to evaluate the expression levels of *IL-33*, *ST2*, and *IL-37* genes in endometrial and endometriotic tissues of women with endometriosis compared to control endometrial tissue.

Materials and Methods: In this case-control study, 11 women with endometriosis and 13 women without endometriosis were enrolled after diagnostic laparoscopy. Written informed consent was obtained from all participants. Ectopic endometrial tissues samples were collected from women with endometriosis during laparoscopy while eutopic endometrial tissues of endometriosis women and endometrial tissues of control women were obtained by pipette. Total RNA was extracted from the endometrial tissues using (TRIzol reagent). Complementary DNA (cDNA) was synthesized using SMOBIO kit. Quantitative real-time PCR (qRT-PCR) was performed using gene-specific primers and SYBR Green Master Mix to analyze the expression levels of the target genes (*IL-33*, *ST2*, *IL-37*) compare to *GAPDH* as the internal control. The relative gene expression was calculated using the $2^{-\Delta\Delta C_t}$ method.

Results: A total of 24 participants were enrolled, including 11 women diagnosed with endometriosis and 13 women in control group. *IL-33*, *IL-33R* (*ST2*) and *IL-37* gene expression were detected in endometrial tissues of endometriosis and control groups. The gene expression levels of *IL-33*, *IL-33R* and *IL-37* were statistically different between three tissue groups (eutopic, ectopic and control endometrial tissues) (*IL-33*: p value: 0.043; *IL-33R*: p value: 0.001; *IL-37*: P: 0.003).

Conclusion: According to this preliminary data, the results showed that increased expression of these genes in endometrial tissues of endometriosis women might be involved in the inflammatory process of this disease.

Keywords: Endometriosis, Endometrium, *IL-33*, *IL-33R* (*ST2*), *IL-37*

P-154: The Effect of N-Acetyl Cysteine on The Expression Levels of *FSHR*, *CYP19A1*, and *PAPP* Genes in Granulosa Cells of Infertile Women with Endometriosis

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Background: Endometriosis affects 5–10% of women of reproductive age and is a prevalent cause of infertility. Oxidative stress, resulting from reactive oxygen species (ROS), disrupts critical pathways such as steroidogenesis and gene expression in granulosa cells. This study aimed to evaluate the effect of the antioxidant drug N-acetylcysteine (NAC) on the expression of the *FSHR*, *CYP19A1*, and *PAPP* genes in the granulosa cells of infertile women with endometriosis.

Materials and Methods: In this randomized, placebo-controlled clinical trial, 29 women with endometriosis were divided into two groups: one receiving NAC and the other receiving a placebo. Following ovarian stimulation, follicular fluid containing granulosa cells was collected, and RNA was extracted. Gene expression levels were measured using real-time PCR.

Results: Baseline parameters, including age, BMI, FSH, LH, TSH, PRL hormones, and ovarian reserve (AMH), showed no significant differences between the groups. However, *CYP19A1* gene expression significantly increased in the NAC group ($P < 0.05$). Although changes in *FSHR* and *PAPP* gene expression were not significant, a positive correlation between *FSHR* and *CYP19A1* expression was observed, suggesting that with larger sample sizes, these differences may become significant.

Conclusion: N-acetylcysteine may enhance oocyte quality and ovarian function in women with endometriosis by increasing the expression of the *CYP19A1* gene. A positive correlation between *FSHR* and *CYP19A1* expression was also observed, suggesting that with larger sample sizes, these differences may become significant.

Keywords: Endometriosis, Infertility, N-acetylcysteine, Reactive oxygen species, Granulosa cells

P-155: Uncovering The Genetic Basis of Idiopathic Familial Primary Ovarian Insufficiency: Insights from Whole Exome Sequencing

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Background: Primary ovarian insufficiency (POI) is characterized by the cessation of ovarian function before 40 years of age and premature depletion of the ovarian reserve. This condition affects approximately 1–4% of women and is clinically manifested by primary or secondary amenorrhea and elevated follicle-stimulating hormone (FSH) levels. Genetic predisposition plays a crucial role, particularly in families with a positive history of POI. This study aimed to investigate genetic variants associated with familial POI using whole-exome sequencing (WES) to enhance the understanding of its underlying genetic determinants.

Materials and Methods: WES was performed on three women diagnosed with idiopathic POI from unrelated probands with a documented history of this disorder in the proband and at least one of the relatives. Variant filtering and classification according to the American College of Medical Genetics and Genomics (ACMG) guidelines was conducted after incorporating data

from multiple databases including NCBI, Ensembl, PubMed, MobiDetails, Franklin, Varsome, GeneCards, MalaCards, Protein Atlas, GTEx, and GnomAD. Variants with low sequencing quality, allele frequency exceeding 1%, low CADD scores, or low expression in relevant tissues were excluded. Candidate variants were validated by polymerase chain reaction (PCR) and subsequent Sanger sequencing in probands and available relatives to confirm segregation.

Results: The analysis identified four pathogenic or likely pathogenic variants, along with eight variants of uncertain significance (VUS), potentially associated with POI. These genes are involved in numerous processes such as embryonic development, cell cycle, immune responses, hormonal regulation, and ovarian function that can lead to POI. Among the identified variants, seven novel variants were discovered in the *ANKRD31*, *NIPBL*, *HPGD*, *VWF*, *NRXN1*, *FLNA*, and *POLE* genes, which had previously been reported as POI candidates. Sanger sequencing confirmed all variants, and segregation analysis confirmed the presence of *ANKRD31* variant in the father and *NIPBL* variant in the mother. Four other genes were identified as novel candidate genes for POI based on existing evidence.

Conclusion: These findings provide novel insights into the genetic architecture of POI by identifying new candidate genes potentially involved in its pathogenesis. The genomic data can facilitate improved genetic counselling and fertility preservation strategies, thereby enhancing reproductive outcomes for affected women.

Keywords: Primary Ovarian Insufficiency, Whole Exome Sequencing, Genetic Variants, Infertility, Sanger Sequencing

P-156: Investigation of ND1 Polymorphisms Utilization to Advance The Ethical Refinement of Mouse Models in Reproductive Research

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Background: Optimizing animal use in scientific research is a core ethical responsibility, guided by the principles of Replacement, Reduction, and Refinement (the 3Rs). Selecting mice with higher reproductive potential may help reduce the number of mice needed in studies. The Mt-ND1 gene, which encodes NADH dehydrogenase 1, is essential for mitochondrial oxidative phosphorylation and cellular energy production which are key factors influencing sperm motility and egg quality. This study investigated ND1 polymorphisms in mice and their potential associations with reproductive outcome, aiming to explore genetic markers that could support more ethical and efficient use of animal models in research.

Materials and Methods: In this study, 200 NMRI mice ,100 VP+ (vaginal plug positive) females and 100 males, were examined for ND1 polymorphisms using Sanger sequencing for Single Nucleotide Variant (SNV) detection. Statistical analyses, including Poisson and Chi-squared tests, were conducted to assess the correlations between ND1 polymorphisms and child-bearing.

Results: Among the 91 identified SNVs in the *ND1* gene, rs33251942 and rs33255684 were the most frequent, each with an allele frequency of 0.3 in the total population, and were always co-present. A comparison between mice carrying both

variants (n=30) and those carrying neither (n=70) showed no significant difference in reproductive outcome (P=0.754), suggesting no association between these variants and fertility status.

Conclusion: Since no statistically significant difference in reproductive outcome was observed between mice with and without the most common ND1 polymorphisms, these variants may not serve as an appropriate factor for guiding ethical refinement of mouse models in reproductive research.

Keywords: Reproduction, Mitochondria, ND1, Mouse Model, Refinement

P-157: HLA Gene Polymorphisms and Ovarian Cancer: A Systematic Review of Genetic Associations and Immune Implications

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Background: Human leukocyte antigen (HLA) polymorphisms are crucial in influencing immune responses and susceptibility to various diseases, including ovarian cancer (OC). These genetic variations can either increase disease risk or provide protective effects.

Materials and Methods: A comprehensive literature search was conducted in April 2024 across five major databases: MEDLINE (PubMed), Web of Science, Scopus, Embase, and Google Scholar. Eligible quantitative studies were independently assessed by two reviewers using the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MASARI).

Results: Decreased expression of HLA class I molecules was frequently observed in OC patients, particularly in individuals carrying the HLA-A*02 allele, which is linked to poor prognosis and immune evasion. HLA class II alleles were associated with tumor invasiveness and disease susceptibility. Non-classical molecules such as HLA-E and HLA-G were found to modulate immune escape mechanisms; HLA-E suppresses natural killer (NK) cell activity, enhancing tumor survival, while the role of HLA-G expression remains complex and context-dependent.

Conclusion: Despite heterogeneity in study populations and HLA polymorphisms analyzed, the evidence suggests that specific HLA variants are linked to ovarian cancer development and mortality rates in certain demographic groups. Understanding these associations may improve diagnostic precision and inform immunotherapeutic strategies.

Keywords: Ovarian Cancer, HLA, Polymorphism, Immune evasion

P-158: Administration of N-acetylcysteine Influence The Expression of Apoptotic Genes in The Granulosa Cells of Infertile Women Diagnosed with Endometriosis

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Background: Endometriosis is a chronic and multifactorial disorder. Reactive oxygen species (ROS) and oxidative stress (OS) contribute to the development of endometriosis, ultimately contributing to decreased fertilization rates and an elevated risk of infertility by influencing the expression of apoptosis-related genes in GCs. Bcl-2, an anti-apoptotic protein, contrasts with BAX, a pro-apoptotic protein, which together culminate in apoptosis. NAC is an antioxidant that has been shown to directly reduce levels of ROS. Additionally, this supplement has the potential to inhibit abnormal cell proliferation and modify cellular behavior from proliferation to differentiation, thereby diminishing endometrial masses.

Materials and Methods: Study design, size, duration: This randomized clinical trial was conducted at the Royan Institute, Tehran, Iran, from 2021 to 2023. Infertile endometriosis women aged between 22 and 38 years, were assigned to receive either NAC or a placebo. The effervescent tablets (NAC 600 mg or placebo) were prepared using identical packaging. Over a period of six weeks, patients were administered 1200 mg of effervescent tablets (2 × 600 mg) daily until ovarian stimulation began to enter the IVF cycle. Participants/materials, setting, methods: The final sample consisted of 7 NAC-treated and 9 placebo-administered patients. Written informed consent was obtained from participants. Blood samples were collected from patients, before and after the intervention to evaluate serum SOD and TAC using ELISA. Additionally, follicular fluid was collected during the puncture procedure. After isolating GCs and extracting their RNA, cDNA was synthesized. Gene expression was done by Real-time PCR for *Bcl-2*, *Bax*, *GAPDH* genes. Statistical analysis was done by independent t test.

Results: Based on the results obtained from this research, the serum levels of TAC before NAC intervention were 0.67 ± 0.21 , and after the intervention, they were 1.03 ± 0.33 . The SOD activities in serum before the NAC intervention were 31.83 ± 13.91 , and after the intervention, they were 38.65 ± 21.72 . Therefore, the serum levels of TAC and SOD increased after treatment in the NAC-treated group ($P=0.031$ and $P=0.467$, respectively). Additionally, the expression level of Bcl-2 increased in NAC-treated patients (0.52 ± 0.350) compared to the placebo group (0.44 ± 0.411), while BAX expression decreased in the GCs of NAC-treated patients (0.37 ± 0.66) compared to the placebo group (0.66 ± 0.490) ($P=0.666$ and $P=0.155$, respectively). Although pregnancy was a secondary outcome in the ongoing randomized controlled trial (RCT), three patients in the NAC-treated group became pregnant, and to date, one live birth has occurred.

Conclusion: The results show that the consumption of NAC supplement can reduce ROS effect and apoptosis in infertile patients with endometriosis.

Keywords: Endometriosis, Apoptosis, Stress Oxidative, N-Acetyl Cysteine

P-159: Evaluation of Genetic Variations of Exon 7 of The Testis-Specific Gene 10 in Iranian Patients with Acephalic Spermatozoa Syndrome

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Background: Acephalic spermatozoa syndrome (ASS) is a rare form of teratozoospermia that causes male infertility, characterized by headless tails, tailless heads, and abnormal head-tail junctions. Structural studies on individuals with ASS have revealed proximal centriole breakage in sperm cells due to Testis-Specific Gene 10 (TSGA10) mutations. This Gene has 21 exons and codes a midpiece protein in sperm that is essential for spermatogenesis. The c.211delG variant in exon 7 of TSGA10 truncates the protein and may impair its function. This ongoing study is the first of its kind conducted in the Iranian population

Materials and Methods: This case-control study was conducted on 10 infertile men diagnosed with ASS, with more than 50% acephalic spermatozoa without a diagnosed genetic cause, and 10 fertile men with normal sperm parameters as controls. After retaining consent, Genomic DNA was extracted from peripheral blood samples using the salting-out method. Polymerase chain reaction (PCR) was performed to amplify target regions of interest. The PCR products were subsequently visualized by agarose gel electrophoresis and sent for Sanger sequencing to detect possible mutations.

Results: Sanger sequencing of the targeted exon revealed no mutations in the studied region of the *TSGA10* gene in any of the participants.

Conclusion: Although previous studies have reported mutations in exon 7 of the *TSGA10* gene in individuals with ASS, no mutations were identified in the targeted exon among the studied patients. Further genetic investigation is recommended to better understand the role of *TSGA10* in this disorder.

Keywords: Male Infertility, ASS, TSGA10, Teratozoospermia, Sanger Sequencing

P-160: Autoimmune-Associated Hub Genes in Sertoli Cell-Only Syndrome: An Integrated Single-Cell Transcriptomic and Network Analysis of LCP2

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Background: Sertoli Cell-Only (SCO) syndrome, a form of

non-obstructive azoospermia (NOA), is marked by complete absence of germ cells in the seminiferous tubules. While its etiology is multifactorial, growing evidence suggests immune dysregulation may contribute to its pathogenesis. This study aimed to identify immune-related hub genes in SCO through integrative transcriptomic analysis and validation.

Materials and Methods: Two single-cell RNA-seq datasets (GSE202647 and GSE154535), including six SCO and three control testicular samples, were analyzed using the Seurat package in R. A total of 831 overlapping differentially expressed genes (DEGs) were identified. A protein-protein interaction network was constructed, and the top 100 hub genes were selected using CytoHubba in Cytoscape. GO and KEGG enrichment analyses were performed. In silico validation was carried out using two RNA-seq datasets (GSE216907, GSE241326) and two microarray datasets (GSE45885, GSE145467).

Results: Among the hub genes, LCP2 was consistently up-regulated in SCO samples across all validation datasets. LCP2 (SLP-76), an adaptor protein in T cell receptor signaling, was enriched in immune-related pathways including T cell and natural killer cell activation. Their expression patterns suggest involvement of both innate and adaptive immunity.

Conclusion: LCP2 may reflect immune-mediated mechanisms contributing to germ cell loss in SCO syndrome. Their consistent dysregulation supports their potential as diagnostic or mechanistic biomarkers.

Keywords: Non-Obstructive Azoospermia, Autoimmunity, Hub Genes

P-161: In Silico Identification of Master miRNA Regulators of CREM and ZBPB Genes in Human Spermatogenesis

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Background: Spermatogenesis is a complex, multi-step process that requires finely tuned gene regulation. MicroRNAs (miRNAs) are known to play essential roles in post-transcriptional regulation during male germ cell development. Identifying shared miRNAs that target key spermatogenesis-related genes may uncover new regulatory mechanisms relevant to male infertility.

Materials and Methods: Two genes with established roles in spermatogenesis—CREM (cAMP-responsive element modulator), a master transcriptional regulator in post-meiotic germ cells, and ZBPB (zona pellucida binding protein), a critical factor in acrosome structure and sperm-oocyte interaction—were selected for analysis. miRNA target predictions were obtained from TargetScan and miRDB databases. For CREM, multiple 3' UTR transcript variants were examined (ENST00000374726.3 and ENST00000469949.2) to ensure transcript-specific accuracy. Only miRNAs predicted by both tools were considered high-confidence candidates. Context++ scores, site types (e.g., 8mer), and target rank/score in miRDB were used to assess prediction strength.

Results: Three miRNAs—hsa-miR-607, hsa-miR-3671, and hsa-miR-590-3p—were predicted by both TargetScan and miRDB to target both CREM and ZBPB. For CREM, binding sites were found in both transcript variants (ENST00000374726.3 and ENST00000469949.2). miR-607 and miR-3671 showed 8mer binding sites at positions 466–473 and 465–472 respectively (ENST00000374726.3), with context++ percentiles of 99. miR-590-3p was predicted to bind at position 411–417 of ENST00000469949.2 with a 7mer-m8 site. All three miRNAs also showed strong binding potential to ZBPB, including 8mer or 7mer-A1 sites in the proximal 3' UTR, with miR-607 ranked 1st in miRDB (score: 95). These results suggest robust and possibly functional miRNA–gene interactions.

Conclusion: Our analysis identified miR-607, miR-3671, and miR-590-3p as potential shared regulators of CREM and ZBPB, two functionally significant genes in spermatogenesis. These findings offer a basis for experimental validation and may contribute to understanding the miRNA-mediated regulatory landscape in male reproductive biology.

Keywords: Spermatogenesis, MicroRNA, CREM, ZBPB, In Silico Prediction

P-162: Absence of Pathogenic Variants in Exon 11 of TSGA10 Gene Among Patients with Acephalic Sperm Syndrome referred to Royan Institute

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Background: Due to the lack of comprehensive epidemiological studies, the exact prevalence of acephalic spermatozoa syndrome (ASS) remains unclear; however, existing case reports indicate that its incidence is likely below 0.1%. ASS is a rare and severe form of teratozoospermia characterized by partial or complete separation of the sperm head from the flagellum, resulting in impaired motility and infertility in affected men. Recent genetic investigations have linked this condition to mutations in several genes involved in sperm head-tail coupling, including *SUN5*, *PMFBP1*, and *TSGA10*. *TSGA10* comprises 21 exons located in the chromosomal region 2q11.2.

Materials and Methods: This study included 10 infertile men with acephalic spermatozoa syndrome, defined by over 50% headless sperm as the case group, and 10 fertile men with normal sperm parameters as the control group. DNA samples were obtained from the Royan Institute DNA bank. PCR was performed, and the products were sequenced. Data were analyzed using FinchTV and compared with reference sequences via NCBI BLAST to detect potential variants.

Results: Exon 11 of the *TSGA10* gene was thoroughly examined; however, no mutations were detected in this exon in any of the patients included in the study.

Conclusion: Consequently, exon 11 is unlikely to be involved in the underlying genetic mechanisms of the syndrome, and future studies are needed in other exons of *TSGA10* and other related genes to achieve a more comprehensive understanding

of its genetic basis.

Keywords: TSGA10, Acephalic Spermatozoa Syndrome, Male Infertility, Spermatogenesis, Genetic Variations

P-163: Induction of Immune-Related Gene Expression by Seminal Exosomes in The Porcine Endometrium

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Background: Seminal plasma (SP) is considered as a vehicle to carry sperm into female reproductive tract, of which functions have not been completely understood. This study aimed to identify the function of seminal exosomes on porcine endometrium.

Materials and Methods: Exosomes were isolated from the sperm-rich fraction of boar semen and were confirmed by the expression of exosome marker HSP70 and size distribution using nano-sight tracking analysis. Porcine endometrial epithelial cells (EECs) were then treated with seminal exosomes, and RNA extracted were subjected to global expression analysis.

Results: Transcripts related to “immune response”, “inflammatory response” and their associated signaling pathways were up-regulated in EECs treated with seminal exosome, whereas those associated with “steroid biosynthesis”, “metabolic pathways” and “T cell differentiation” were down-regulated. The decrease in PMVK, SC5D, INSIG1, HSD17B7, NSDHL, HMGCR, SQLE and FDFT1, and increase in CCL20, TNFSF15, AMCFII, CXCL2 and CXCL8 were also found in the endometrium from the naturally mated pigs. Moreover, changes in exosome-induced CYP24A1, EBP, CCL20, AMCFII and IL1A expression were not regulated by the exosome removed SP.

Conclusion: These observations indicated that exosomes present in SP are involved in the immune-related gene regulation in the uterus, which could pave the passage for sperm and possibly fertilized eggs.

Keywords: Seminal Plasma, Exosomes, Endometrium, Porcine Immune-Related Genes

P-164: Exploring Molecular Links Between Two Oocyte-Related Transcription Factors in The Context of Endometriosis

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Background: In our previous study conducted at Royan Institute, we demonstrated significant downregulation of two oocyte maturation-related transcription factors, Orthodentical Homeobox 2 (OTX2) and SRY-BOX Transcription Factor 15 (SOX15), in both Cumulus cells and follicular fluid of women with endometriosis compared to non-endometriotic controls (n=30 per group, P<0.0001). This decrease was in line with clinical data regarding the Metaphase 2 (MII) oocyte rate in women with endometriosis. Therefore, it seems that OTX2 and SOX15 expression levels in Cumulus cells and follicular fluid may offer a novel approach to predict oocyte quality and developmental competence in endometriosis-affected women. This secondary analysis aimed to explore potential correlations between these genes and relevant clinical parameters and to assess their functional associations through protein interaction network analysis.

Materials and Methods: Correlation analyses were performed using either Pearson or Spearman tests based on data distribution assumptions using GraphPad Prism (V 9.0.0) to evaluate the relationships between gene expression levels (in both sample types), age, body mass index (BMI), and number of MII oocytes. Bioinformatic interaction networks were constructed using STRING and GeneMANIA databases.

Results: A significant positive correlation was observed between OTX2 and SOX15 expression in Cumulus cells (r = 0.6047, P=0.0004), whereas no significant associations were found between gene expression and age, BMI, or MII oocyte rate. Network analysis revealed that OTX2 and SOX15 interact indirectly through Octamer-Binding Protein 4 (OCT4), another transcription factor involved in oocyte maturation.

Conclusion: All three genes are co-expressed and functionally enriched in the WNT/β-catenin signaling pathway—a pathway critically involved in folliculogenesis and disrupted in endometriosis. This integrative analysis suggests a cooperative role for OTX2 and SOX15, potentially mediated by OCT4 and the WNT/β-catenin axis. These findings underscore the potential contribution of this gene network to impaired oocyte quality in endometriosis and highlight targets for future functional validation.

Keywords: Endometriosis, Cumulus Cells, Transcription Factors, Gene Expression Correlation, Protein Interaction Network

P-165: Relationship between IUI Outcome and BAG6 Gene Expression in Sperm

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Background: Infertility significantly affects couples' quality of life. Intrauterine insemination (IUI) is a widely used cost-effective infertility treatment that closely resembles natural conception but has a low success rate (10–15%). BCL-2 associated athanogen 6 (BAG6), as a multifunctional chaperone protein, plays a vital role in sperm integrity and male fertility by stabilizing heat shock protein A2 (HSPA2). BAG6 supports spermatogenesis, sperm maturation, and zona pellucida binding, while its dysregulation is linked to oxidative stress, DNA damage, and reduced sperm function. This study investigates BAG6 gene expression in sperms of men whose partners are undergoing IUI.

Materials and Methods: This cohort study includes 300 infertile men (BMI ≤ 30 kg/m², age ≤ 45 years old) whose wives are undergoing IUI at Royan Institute. On the IUI day, semen samples are collected and sperms are separated. Based on chemical pregnancy results, samples are divided into IUI success and IUI failure groups. BAG6 gene expression in sperms is evaluated using Real-Time RT-PCR after RNA extraction and cDNA synthesis. β -actin serves as the housekeeping gene. Data are analyzed with SPSS using independent t-tests and results are reported as mean $\pm$ standard deviation (SD). A P less than 0.05 is considered statistically significant.

Results: Up to now, 12 men are enrolled. Gene expression level of BAG6 showed no significant difference between IUI-failure and IUI-success groups.

Conclusion: BAG6 has been reported as biomarker for predicting unexplained infertility. However, according to these preliminary data, no association was found between BAG6 gene expression level in sperm and IUI outcome. A definite conclusion will be made after completion of the study.

Keywords: Infertility, IUI, Sperm, BAG6, Gene expression

P-166: The Relationship between Vitamin D Receptor (VDR) rs731236 Genetic Variant and Recurrent Miscarriage

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Background: Miscarriage is one of the most common problems during pregnancy, which occurs in approximately 1-3% of pregnancies. Various reasons affect pregnant women with this multifactorial disease. However, in 50% of cases, the cause of abortion is not known. Many studies report a significant association of single-nucleotide polymorphism (SNP) changes of genes involved in the pathways related to fetal development with recurrent miscarriage. One of the candidate genes that has recently received attention is the *VDR* (Vitamin D receptor) gene. Considering the role of vitamin D in the reproductive system of women and since its receptors have been found throughout the reproductive system in the ovary, endometrium and

placenta, polymorphism in this gene may be associated with recurrent miscarriage in women. The purpose of this study is to investigate the relationship between polymorphism rs731236 (Taql1) of the vitamin D receptor gene and recurrent miscarriage in Iranian women referred to Royan Research Institute.

Materials and Methods: In this case-control study, 57 women with a history of recurrent miscarriage and 57 women without a history of recurrent miscarriage were selected. The rs731236 polymorphism of the *VDR* gene was investigated by PCR-RFLP method and Chi squared test (X²) and SPSS software were used to analyze the data and compare the frequency of genotypes and alleles in the two studied groups.

Results: Among the 57 women in the control group, TT genotype, TC genotype, and CC genotype accounted for 40.3%, 45.6%, and 14%, respectively. Among the 57 women in the patient group, TT genotype accounted for 28%, TC genotype accounted for 52.6%, and 19.3% had CC genotype. In the population of the patient group, the frequency of T allele is equal to (54.39) and the frequency of C allele is (45.61), and in the control group, the frequency of T and C alleles is (63.16) and (36.84), respectively.

Conclusion: This study did not find a significant association between the *VDR* rs731236 genetic variants and recurrent miscarriages.

Keywords: Recurrent Miscarriage, Single-Nucleotide Polymorphism, Vitamin D Receptor, Restriction Fragment Length

P-167: Systematic Review: lncRNAs and circRNAs in Decidualization and Recurrent Implantation Failure Outcomes

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Background: Recurrent implantation failure (RIF) is often caused by issues in decidualization and endometrial receptivity. Long non-coding RNAs (lncRNAs) and circular RNAs (circRNAs) are important in controlling these processes as they act as epigenetic factors.

Materials and Methods: Our study set out to investigate how lncRNAs and circRNAs contribute to the molecular pathways involved in decidualization and endometrial receptivity in women with RIF. To find relevant research, we explored PubMed, Scopus, Web of Science, and Embase up to June 2025. We focused on studies that looked at the expression, roles, or regulatory networks of lncRNAs and circRNAs in RIF or recurrent miscarriage. We assessed study quality using tools like the Newcastle-Ottawa Scale and QUADAS-2, grouping them by their risk of bias. Since the studies varied widely in design and data, we used a narrative approach to combine their findings through common themes.

Results: From 25 studies, we found that elevated HOXA11-AS and H19 interfere with Wnt/ β -catenin and HOXA10 pathways, disrupting decidualization and endometrial receptivity. In RIF cases, increased lncRNAs reduce receptivity by affecting cell adhesion. In particular, ceRNA networks, including TRG-AS1, NEAT1, and circRNA_0001721, modulate receptivity via angiogenesis. Additionally, increased prokineticin 2 suppresses MMP9 expression, hindering endometrial remodeling.

Conclusion: This study shows that lncRNAs and circRNAs

play a major role in decidualization problems in RIF, especially by influencing Wnt/ β -catenin and ceRNA networks, and indicates their possible use as biomarkers.

Keywords: lncRNA, CircRNA, Decidualization, RIF, CeRNA Networks

P-168: Genetic Screening of The c.1739A>C Variation in TSGA10 in Patients with Acephalic Spermatozoa Syndrome

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Background: *TSGA10* (testis-specific gene 10) is a testis-specific gene and plays an important role in spermatogenesis and structural integrity of the spermatozoon. Different variations in this gene have been shown to play a role in causing acephalic spermatozoa syndrome (ASS), a rare but severe form of teratozoospermia leading to male infertility. *TSGA10* consists of 21 exons, and exon 18 has been reported to contain a pathogenic variant, c.1739A>C. This variant has been described as a novel homozygous missense mutation that leads to a significant reduction or absence of *TSGA10* protein expression in the spermatozoa of affected individuals

Materials and Methods: This case-control study was performed on 20 male participants, including 10 infertile men diagnosed with acephalic spermatozoa syndrome, who had more than 50% acephalic spermatozoa and lacked any known genetic variants associated with the disorder. Following genomic DNA extraction using the salting-out method, polymerase chain reaction (PCR) was performed on the collected samples. In the next step, the resulting PCR products are sent for Sanger sequencing. The results were analyzed using FinchTV, and the obtained sequences were compared with reference sequences using NCBI BLAST to identify potential variants.

Results: Sanger sequencing of exon 18 of the *TSGA10* gene in both case and control groups revealed no presence of the target variant or any other variants in any of the studied individuals.

Conclusion: These findings suggest that mutations in exon 18 of the *TSGA10* gene are not a prevalent contributor to acephalic spermatozoa syndrome in the Iranian studied cases.

Keywords: Male Infertility, *TSGA10*, Acephalic Spermatozoa Syndrome, Teratozoospermia

P-169: Identification of Genetic Variants Related To Idiopathic Familial Primary Ovarian Insufficiency Using Whole Exome Sequencing

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Background: Primary ovarian insufficiency (POI) is a condition marked by amenorrhea, reduced follicles and impaired follicular function before age of 40. While 70-90% of cases are idiopathic, genetic factors contribute to 20-25% of cases. This study was aimed to identify genetic factors associated with POI in patients with family history.

Materials and Methods: Whole exome sequencing (WES) data analysis was performed with predictive bioinformatics tools to identify genes associated with POI in three idiopathic patients. Variants were classified based on ACMG guidelines. NCBI, Malacard, GTEx, Human Protein Atlas, OMIM, Marvel, GeneCard, Franklin, Varsome and MobiDetails tools and databases were used for variants interpretation. Finally, after designing primers and performing polymerase chain reaction (PCR), Sanger Sequencing was utilized to confirm potentially causal variants.

Results: In the studied probands, we identified 11 variants associated with POI. Of these, one was pathogenic, four were likely pathogenic, and six were of uncertain significance. Variants found in *GALT*, *HFM1*, *WDR11*, *LRP5*, *RELN* and *PLB1* are considered novel variants as they have not been reported in POI so far. The other five were considered as novel candidate genes that have not been previously reported in POI. Animal model studies on mouse ovarian tissue indicate that mutations in these genes can lead to folliculogenesis defects (*RELN*), impaired fertility (*GALT*), and disrupted germ cell growth (*LRP5*), reduced follicular reserve (*HFM1*), *POF* (*PLB1*), and hypogonadotropic hypogonadism (*WDR11*).

Conclusion: The identified genes are involved in hypogonadism, disrupting meiosis and gamete production, oocyte maturation, germ cell development, ovarian follicle function, menstrual cycle changes, and ovulation. Considering the role of several genes in the occurrence of POI, this disease is oligogenic. This study highlights the importance of WES in finding etiology of idiopathic POI and potential in prevention and treatment plans.

Keywords: Primary Ovarian Insufficiency, Whole Exome Sequencing, Family History, Genetic Variants

P-170: Paternal Role of Annexin A5/M2 Haplotype Carriage in Unexplained Recurrent Implantation Failure (uRIF)

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Background: Unexplained Recurrent implantation failure

(uRIF) indicates the failure to achieve pregnancy after at least 3 cycles of transferring good-quality embryos, despite of no clear cause. Multiple embryonic and parental factors could contribute to pathogenesis of RIF, including parental chromosomal abnormality, uterine anomalies, hormonal factors and hereditary coagulation disturbances. Annexin A5 (ANXA5) is involved in membrane stability and coagulation. The M2 haplotype of ANXA5 associates with reduction in its activity, thus predisposing to RIF. This study aims to investigate the frequency of ANXA5/M2 haplotype in Iranian couples suffering from uRIF. **Materials and Methods:** In this case-control study, RIF was defined as more than 3 failed IVF/ICSI cycles in couples with maternal and paternal ages of less than 40 and 45, respectively. The uRIF couples were screened for any etiologic factors that could contribute to etiology. Fertile couples who were referred for sex selection of their next child were considered as control group. After signing written consents and peripheral blood samples from both groups were collected, which was followed by DNA extraction, PCR, and Sanger sequencing.

Results: In this ongoing study, 21 uRIF and 22 fertile couples were enrolled out of 30 intended couples. ANXA5/m2 haplotype was observed in three men in the uRIF group (13.64%) and only one man (4.55%) in the control group ($P>0.05$), although this threefold increase was not statistically significant. This haplotype was not found in women of either group.

Conclusion: Although the frequency of the ANXA5 M2 haplotype did not differ significantly between the two groups under study, it's notable that this haplotype was observed only in male partners of uRIF and controls. Given Annexin A5's properties, the paternal presence of the M2 haplotype may affect sperm membrane integrity or early zygotic signaling, which may influence RIF.

Keywords: Infertility, Haplotypes, Annexin A5, IVF failure, Recurrent Implantation Failure

P-171: hsa_circ_0004712 Downregulation in Recurrent Implantation Failure: Insights into IVF Outcome Prediction

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Background: Recurrent implantation failure (RIF) remains a major obstacle in assisted reproductive technologies, defined by the repeated inability to achieve successful embryo implantation following the transfer of high-quality embryos in *in vitro* fertilization (IVF) cycles. IVF treatments are often costly, emotionally taxing, and psychologically burdensome. Despite advances in reproductive medicine, the precise molecular mechanisms underlying RIF are still not fully understood. Emerging studies indicate that non-coding RNAs (ncRNAs), particularly circular RNAs (circRNAs), play essential regulatory roles in embryo implantation. Due to their covalently closed-loop structure, circRNAs are highly stable and resistant to degradation, making them promising candidates for non-invasive biomarkers in biological fluids such as blood, urine, and saliva.

Materials and Methods: Peripheral blood samples were collected from 60 women undergoing IVF treatment at Tabriz Valiasr Hospital between June 20, 2024, and March 20, 2025. Participants were divided into two groups: 30 women with RIF and 30 age-matched women with successful implantation serving as controls. Quantitative real-time PCR (qRT-PCR) was

performed to assess the expression levels of hsa_circ_0004712. Bioinformatics analyses were also conducted to predict target miRNAs and explore potential circRNA-miRNA-mRNA interaction networks. Additionally, the expression of PDE7B, the host gene of hsa_circ_0004712, was evaluated in both groups.

Results: qRT-PCR analysis revealed a significant downregulation of hsa_circ_0004712 in the RIF group compared to the control group. Correspondingly, the expression of PDE7B was also markedly reduced in women with RIF. Bioinformatics data supported the involvement of the hsa_circ_0004712-miRNA-mRNA axis in biological pathways potentially implicated in implantation failure.

Conclusion: The significant downregulation of hsa_circ_0004712 and its host gene PDE7B in women with recurrent implantation failure suggests a potential regulatory role in embryo implantation. These findings highlight the diagnostic potential of hsa_circ_0004712 as a non-invasive biomarker for RIF in IVF patients.

Keywords: Recurrent Implantation Failure, Circular RNA, hsa_circ_0004712, Non-Coding RNA, IVF

P-172: The Effect of L-carnitine and Silver Nanoparticle on The Expression of Androgen Receptor Gene in a Polycystic Ovary Syndrome (PCOS) Mouse Model

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Background: Polycystic ovary syndrome (PCOS) is a hormonal disorder frequently linked to metabolic abnormalities in reproductive aged women. It is accompanied by an increase in androgen and polycystic ovaries. L-carnitine (LC) has immense functional capabilities to regulate the oxidative and metabolic status of the female reproductive system. The aim of this study was to evaluate the effect of L-carnitine and silver nanoparticle on the expression of androgen receptor gene.

Materials and Methods: In this study, for inducing the polycystic ovary phenotype, female mice were injected daily with testosterone enanthate for 4 weeks. Then, these mice were randomly allocated into 9 groups: PCO, Sham (PCO + normal saline), PCO+ LC (250 mg/Kg, i.p.), PCO + nanoparticles (0.5, 0.75, 1 ppm, i.p., twice a week for 4 week), and PCO + LC+ nanoparticle. All groups also compared with control group that received only standard food. At the end, the ovaries from all groups were removed and the ovarian total RNA was extracted for analyzing the expression of androgen receptor gene.

Results: Our results showed that the expression of androgen receptor gene was upregulated in the PCO groups compared to the control group. After treatment with silver nanoparticle and L-carnitine, a significant reduction in the expression level of AR gene was observed ($P<0.05$).

Conclusion: Based on these results, silver nanoparticles and L-carnitine may help treat PCOS and its complications through various mechanisms, including the modulation of androgen receptor gene expression, thereby serving as a potential therapeutic strategy for patients with polycystic ovary syndrome

Keywords: PCO, L-Carnitine, Silver Nanoparticle, Androgen Receptor Gene Expression

P-173: Sphingolipid Gene Expression Dynamics in Human Folliculogenesis: Implications for Oocyte Maturation and Fertility

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Background: Sphingolipids have become the focus of several fields of research in the medical and biological sciences, as these bioactive lipids have been identified as potent signaling and messenger molecules. Research has also shown that changes in the expression of sphingolipid genes have detrimental effects on folliculogenesis, oocyte maturation, and fertility.

Materials and Methods: Transcriptomic data from a publicly available dataset (GSE107746) on human oogenesis/folliculogenesis were analyzed. After preprocessing and quality control, differentially expressed genes (DEGs) were identified across various stages of folliculogenesis (primordial, primary, secondary, and preovulatory) in oocytes and granulosa cells.

Results: DEG analysis of the transcriptome in oocytes and granulosa cells at different stages of folliculogenesis revealed changes in the expression of sphingolipid genes (*DEGS2*, *SMPD3*, *ELOVL1*, *FADS2*) between the primordial-preovulatory, primary-preovulatory, and secondary-preovulatory groups. Enrichment analysis indicated these genes are involved in sphingolipid metabolism, signaling pathways, and fatty acid metabolism.

Conclusion: Sphingolipid gene expression dynamics were notably altered between early follicular stages and the preovulatory phase. Genes down-regulated in oocytes compared to granulosa cells may contribute to granulosa cell proliferation or oocyte meiotic arrest, while up-regulated genes in oocytes may be linked to oocyte maturation. These findings underscore the potential role of sphingolipids in regulating key events during folliculogenesis.

Keywords: Sphingolipids, Folliculogenesis, Gene expression, Fertility, Bioinformatics

P-174: Investigating Interleukin-6 and Long Non-coding RNA MALAT1 Expression in Granulosa Cells: Insights into PCOS Pathophysiology

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Background: Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder among women of reproductive age, marked by hormonal imbalances and disrupted ovarian function. Granulosa cells (GCs) are integral to follicular development and oocyte maturation. Recent studies suggest that long non-coding RNAs (lncRNAs), such as MALAT1, and cytokines like interleukin-6 (IL-6) play significant roles in ovarian physiology and may contribute to the pathogenesis of PCOS.

Materials and Methods: This study involved 26 women with PCOS and 17 healthy women experiencing infertility due to male factors, all attending the infertility center at Beheshti Hos-

pital in Kashan. Granulosa cells were isolated from follicular fluid obtained during oocyte retrieval procedures. Total RNA was extracted, and complementary DNA (cDNA) was synthesized. Quantitative real-time PCR (qRT-PCR) was employed to assess the expression levels of MALAT1 and IL-6. Statistical analysis was performed using the unpaired t-test with Welch's correction.

Results: The analysis revealed a significant downregulation of MALAT1 expression in granulosa cells from women with PCOS compared to controls ($P=0.0003$). In contrast, IL-6 expression levels did not show a significant difference between the two groups ($P=0.8439$).

Conclusion: The observed decrease in MALAT1 expression in granulosa cells of PCOS patients suggests a potential involvement of this lncRNA in the molecular mechanisms underlying the syndrome. The unchanged IL-6 expression indicates that its role may be limited in the context of granulosa cell function in PCOS. These findings underscore the need for further research to elucidate the precise roles of MALAT1 and IL-6 in ovarian physiology and their implications in PCOS pathogenesis.

Keywords: Polycystic Ovary Syndrome, Granulosa Cells, MALAT1 Long Noncoding RNA, Interleukin-6

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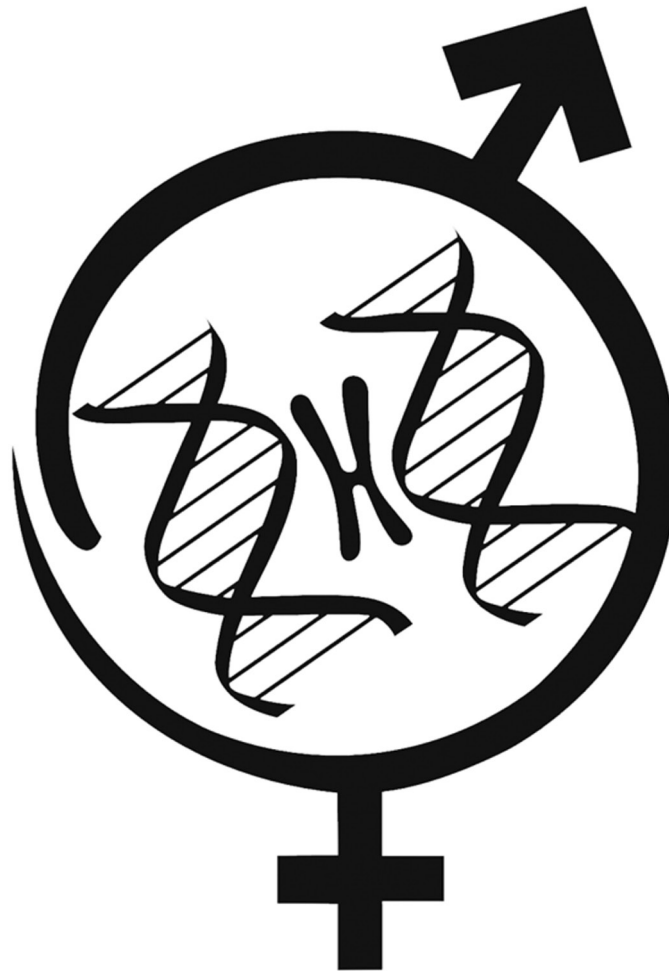
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Abstracts of
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Reproductive Biomedicine Research Center
Tehran, Islamic Republic of Iran

Invited Speaker

Inm-1: Ovarian Sclerotherapy for Endometrioma: A Fertility-Preserving Minimally Invasive Approach

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Background: Ovarian sclerotherapy is an ultrasound-guided procedure involving cyst aspiration followed by instillation of a sclerosing agent (typically 95-99% ethanol or polidocanol) to ablate the endometrioma epithelium. It offers a critical fertility-sparing alternative to cystectomy, particularly valuable for infertility patients with diminished ovarian reserve (DOR) or recurrent cysts.

Key Advantages:

1. Ovarian Reserve Preservation: Significantly less AMH decline vs. cystectomy (10-20% vs. 40-60%), avoiding cortical stripping.
2. Reduced Recurrence: Recurrence rates (5-25%) are markedly lower than aspiration alone (>60%) and comparable to cystectomy in recent RCTs.
3. Minimal Invasiveness: Outpatient procedure under local anesthesia.

Technical Evolution:

- Short Ethanol Retention (10-30 minutes) is now standard, proving equally effective to prolonged exposure while reducing pain and complications.
- Polidocanol (1-3%) shows promise as a less painful alternative to ethanol, though ethanol remains gold standard.

IVF Integration:

- Effectively manages cysts pre-IVF (allowing ovarian recovery), during oocyte retrieval (single-procedure efficiency), or post-failed cycles.
- May improve ovarian response and reduce IVF contamination risks versus leaving large cysts in situ.

Safety:

Major complications are rare (<1-2%). Transient pelvic pain (ethanol-related) is common; serious risks (abscess, chemical peritonitis) are mitigated by precise technique and volume control (≤80% cyst volume). Weight-based ethanol dosing is critical to avoid toxicity.

Current Status:

Recognized in ASRM guidelines (2023) as a valid option, especially for DOR patients or cystectomy contraindications. Long-term fertility data (>5 years) remain an active research focus.

Conclusion: Sclerotherapy balances efficacy, ovarian preservation, and safety, establishing itself as an essential tool in the fertility specialist's arsenal for endometrioma management.

Inm-2: Prevention and Management Strategies for Ovarian Hyperstimulation Syndrome (OHSS) in Patients with Polycystic Ovary Syndrome (PCOS)

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Ovarian hyperstimulation syndrome (OHSS) represents a se-

rious and potentially life-threatening complication of assisted reproductive technologies. Patients with polycystic ovary syndrome (PCOS) are at higher risk of developing severe forms of this syndrome due to unique pathophysiological characteristics including increased ovarian reserve, hypersensitivity to gonadotropins, and associated metabolic disorders. This comprehensive systematic review aims to evaluate the most effective primary and secondary prevention strategies along with optimal management approaches for OHSS in this high-risk patient population. This systematic review involved extensive searches of reputable scientific databases to evaluate all controlled ovarian stimulation protocols and interventional strategies related to OHSS prevention and management in PCOS patients. Assessment criteria included: efficacy of modified stimulation protocols (incorporating GnRH antagonist protocols with low-dose gonadotropins), alternative ovulation trigger strategies (using GnRH agonist instead of hCG), adjunctive approaches like systematic freeze-all embryo cryopreservation, and the impact of adjuvant therapies such as metformin in insulin-resistant patients. The value of rigorous biochemical monitoring (serum estradiol levels) and ultrasound findings in OHSS prevention was also analyzed. Comprehensive analysis of studies demonstrated that modified stimulation protocols using low-dose gonadotropins (75-150 IU) combined with GnRH antagonists significantly reduced OHSS incidence ($P<0.05$). Replacing hCG with GnRH agonist for ovulation triggering in antagonist protocols decreased OHSS risk by 70%. The freeze-all strategy not only prevented pregnancy-associated OHSS but also improved treatment success rates. Metformin administration (1500-2000 mg/day) in insulin-resistant PCOS patients modulated ovarian response and reduced OHSS occurrence by 40%. For established OHSS cases, timely interventions including targeted fluid therapy with normal saline, intravenous albumin (25-50 g), and ultrasound-guided paracentesis combined with careful renal and respiratory monitoring proved most effective. Evidence-based preventive protocols incorporating modified stimulation regimens, GnRH agonist triggering, planned freeze-all strategies, and metformin adjunct therapy can minimize severe OHSS occurrences in at-risk PCOS patients. Healthcare team education on early recognition and continuous monitoring of high-risk patients are crucial components of successful prevention and management. Integrating these strategies into standard infertility treatment protocols for PCOS patients can simultaneously enhance both treatment safety and efficacy.

Inm-3: The Effect of Bacterial and Viral Infections on ART Results

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Viral, bacterial, spirochetal, chlamydial and mycobacterial infections can affect fertility and ART. Infections may act with variable impact on the physiopathology of the reproductive organs, determining infertility or reducing the outcomes of assisted reproduction technology. Infectious diseases can negatively impact the success rates of assisted reproductive technology (ART) such as *in vitro* fertilization (IVF). Specifically, infections can affect embryo implantation, pregnancy rates,

and increase the risk of miscarriage. Viral hepatitis, as well as HIV, can reduce sperm quality. Syphilis carries a risk of erectile dysfunction and increased endometrial thickness. Chlamydia is the main cause of pelvic inflammatory disease. In relation to Mycoplasma and Ureaplasma spp., only few species seem to show a correlation with infertility and poor *in vitro* fertilization outcomes. STIs like chlamydia and gonorrhea can cause pelvic inflammatory disease (PID), which can lead to tubal damage and hinder implantation. There is evidence of a role for bacterial vaginosis in early pregnancy loss. HPV infection in males seems to determine infertility. Herpesviruses are more a risk for fetuses than for fertility itself. Zika virus is responsible for altered early embryo development and waiting to conceive is recommended in suspected or confirmed cases. The impact of SARS-CoV-2 is yet to be elucidated. Rubella and toxoplasmosis can provoke important congenital defects and therefore screening is mandatory before conception; a vaccine for Rubella is recommended. Systemic infections can have a broad impact, infections cause fever and inflammation throughout the body can also negatively affect the ovaries and uterus, impacting egg quality, fertilization, and implantation. Further and well-designed studies are still needed to better elucidate the role of some infectious agents, to improve fertility and its treatments.

Inm-4: The Role of Artificial Intelligence in Infertility Diagnosis and Treatment

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Artificial Intelligence (AI) is revolutionizing the evaluation and management of male infertility by introducing precision, automation, and objectivity into sperm analysis. One of the most significant advancements is in motility assessment. Modern AI-based systems utilize frame-by-frame video tracking and deep learning models—such as the AI Sperm Image Tag platform—to analyze individual sperm trajectories in real-time. These systems can classify sperm motility into progressive, non-progressive, and immotile categories with superior accuracy compared to manual methods, enabling consistent and reproducible diagnostics. In morphology assessment, AI combined with label-free holographic imaging eliminates the need for staining, thus preserving sperm viability. High-resolution digital holography captures 3D structural data of live sperm, which is then processed using convolutional neural networks (CNNs) to detect abnormalities in the head, midpiece, and tail. This non-invasive technique enhances accuracy while allowing simultaneous analysis of both morphology and motility on live samples. Sperm counting has also been transformed through AI-powered image recognition algorithms that can automatically identify and quantify sperm in large datasets with minimal human input. These tools significantly reduce inter-observer variability and human error. Furthermore, AI is aiding embryologists in selecting the optimal sperm for ICSI. By analyzing live video feeds in real-time, AI algorithms can score and rank sperm cells based on multi-parameter characteristics, streamlining the selection process and potentially improving ART outcomes. Together, these AI-driven innovations mark a paradigm shift in male infertility care—offering faster, more reliable, and non-invasive diagnostic tools that improve both clinical workflow and patient outcomes.

Inm-5: Reproductive Medicine with The Help of Artificial Intelligence

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In the past few years, artificial intelligence has experienced rapid growth and has reached the stage of implementation in various applications, including health. Advances in learning algorithms and theories, the availability of large data sets, and improved computing power have contributed to advances in current applications of artificial intelligence. Machine learning, a subset of artificial intelligence, allows computers to automatically identify patterns from large and complex data sets and use these patterns to make predictions. Artificial intelligence is increasingly applicable in healthcare, and numerous machine learning methods have been used to improve advanced infertility treatments. In this presentation, we discuss various aspects of artificial intelligence and machine learning and address the applications, limitations and potential challenges of using artificial intelligence in improving advanced infertility treatments.

Inm-6: Patient-Centered Care and AI: A Transformative Partnership in Modern Healthcare

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The intersection of patient-centered care and artificial intelligence represents a pivotal evolution in healthcare delivery. While medical advancements have significantly extended life expectancy, they've simultaneously introduced complex challenges including demographic shifts toward an aging population, the growing burden of chronic diseases, overextended healthcare professionals, and heightened patient expectations for personalized treatment. AI emerges as a powerful enabler in this landscape, offering four key advantages: enhanced diagnostic accuracy through advanced imaging and wearable data analysis, truly personalized treatment plans based on genetic and lifestyle factors, improved clinical communication via intelligent virtual assistants, and significant reductions in administrative burdens through automation. However, this transformation faces substantial barriers including data privacy concerns, the need for algorithmic transparency, and the crucial preservation of human connection in medical care. A strategic implementation framework proves essential for successful adoption, beginning with comprehensive needs assessment to identify institutional priorities, followed by carefully controlled pilot programs such as medication management systems or patient communication chatbots. This phased approach allows for valuable experience while mitigating risk. Subsequent stages should emphasize extensive training for all stakeholders, gradual scaling of successful applications, and continuous performance evaluation through both quantitative metrics and qualitative feedback. For optimal integration, the healthcare sector must prioritize workforce education, establish robust ethical guidelines, and support ongoing research into AI's long-term

impacts. When thoughtfully implemented, this synergy of AI and patient-centered principles promises not only greater clinical efficiency but also a more compassionate, individualized healthcare experience that maintains the essential human element at its core. The future of healthcare thus lies not in choosing between technology and humanity, but in their thoughtful integration to serve patients more effectively.

Inm-7: Artificial Intelligence in Medicine: Navigating Ethical, Legal and Technical Limitations

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The integration of artificial intelligence (AI) into medical practice introduces transformative potential but faces multidimensional barriers spanning technical, ethical, and regulatory domains. This keynote analyzes the critical limitations of AI in healthcare and proposes governance frameworks to ensure safe adoption.

Key Challenges:

1. Ethical Dilemmas:

- o Data privacy risks in AI-driven diagnostics and patient monitoring systems.
- o Black-box decision-making undermining clinician trust and accountability.
- o Bias amplification in algorithms trained on non-representative datasets.

2. Legal Complexities:

- o Ambiguous liability for AI-assisted misdiagnoses (clinician vs. developer responsibility).
- o Non-standardized validation of AI tools across jurisdictions.

3. Technical Barriers:

- o Interoperability gaps between AI systems and hospital IT infrastructures.
- o Cybersecurity threats (e.g., adversarial attacks on medical imaging algorithms).

Governance Solutions:

• Three-tier regulatory model:

1. Government: Mandates core standards (e.g., data security, algorithmic transparency).
2. Independent bodies: Technical audits and certification (e.g., FDA-like evaluation).
3. Industry: Self-regulation with continuous compliance reporting.

- Explainability-by-design requirements for clinical AI models.
- On-device AI processing to mitigate cloud-dependent privacy risks.

Economic & Insurance Adaptations:

- Dynamic pricing models for AI services (accuracy-based vs. time-based tariffs).
- Hybrid insurance schemes covering AI-related liabilities (e.g., misdiagnosis, data breaches).

Conclusion: By addressing these limitations through structured governance and cross-sector collaboration, AI can augment—not replace—human expertise while safeguarding patient rights.

Inm-8: Endocrine Disorders Affecting Sexual Health and Fertility

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Endocrine disorders can significantly affect sexual health and fertility in men and women. Common endocrine disorders such as polycystic ovary syndrome (PCOS), thyroid disorders, and diabetes can disrupt the hormonal balance necessary for reproductive function and lead to menstrual disorders, impotence, and infertility. Polycystic ovary syndrome: PCOS is one of the main causes of female infertility, characterized by hormonal imbalance (increased androgens), irregular periods, and anovulation (absence of ovulation). In addition to anxiety, depression, which is more common in women with polycystic ovary syndrome and can significantly affect sexual performance and satisfaction, hormonal imbalance and clinical symptoms of PCOS such as increased hair loss and acne can negatively affect women's self-confidence and sexuality. Thyroid Disorders: Thyroid disorders can significantly affect health and sexual performance in both men and women. Both hypothyroidism and hyperthyroidism can lead to various forms of sexual dysfunction, including decreased libido, erectile dysfunction, vaginismus, and sexual satisfaction. They can also disrupt the menstrual cycle and affect ovulation and fertility. Diabetes: It can significantly affect sexual health in men and women. Erectile dysfunction, decreased sexual desire and painful intercourse are among the most common sexual dysfunctions of diabetes. These problems are caused by nerve damage (neuropathy) and blood vessel damage caused by diabetes (microvascular complications) that affect arousal, sexual function and fertility. Treatment options vary depending on the specific condition and may include hormone replacement therapy, medication to regulate hormone levels, lifestyle modifications, and blood sugar control.

Inm-9: Psychological Factors Affecting Sexual Health

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The goal of psychosexual therapy is to change the psychological processes that cause sexual problems. Making changes in the predisposing (personality; trait affect; sexual Beliefs), precipitant (for example, professional or emotional failure), and maintaining (performance anxiety; negative thoughts and emotions; avoidance of intimacy) processes will ultimately lead to changes in sexual function. Over the last half century, various models have been proposed to explain the impact of these determinants. While Masters and Johnson emphasized performance anxiety and the phenomenon of spectating (self-focused attention), Barlow and Nobre explained cognitive-affective and cognitive-emotional models, respectively. Despite the acceptance of the Masters and Johnson model and their therapeutic interventions during the 1970s, which were based on sensate focus (a type of systemic desensitization), therapists gradually encountered complex cases that did not respond appropriately to treatment. More recent studies suggest that cognitive variables have a mediating and moderating role on the relationships between other predictive factors (such as medical, relational, psychopathologies, and sexual response).

Inm-10: Environmental Pollution and Its Impact on Reproductive Health

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Environmental pollutants, encompassing chemical, biological, and physical agents, are recognized as a global challenge with profound implications for human health, particularly sexual and reproductive health. These pollutants include heavy metals (such as lead, cadmium, and mercury), particulate matter, phthalates, and bisphenol A (BPA), which affect reproductive processes through mechanisms like endocrine disruption, increased oxidative stress, and inflammation. Phthalates, used as plasticizers in materials like PVC, and BPA, a key component in polycarbonate and epoxy resin production, can leach into food and beverages, interfering with hormonal metabolism. In women, oogenesis is highly vulnerable due to the limited number of oocytes and the ovary's sensitivity to toxins, especially from embryonic stages to adulthood. These pollutants can reduce ovarian reserve, cause hormonal imbalances, and lead to premature birth, spontaneous abortion, and fetal defects. Studies have shown that high levels of phthalates (e.g., MEHP) and BPA are associated with reduced antral follicle counts, embryo implantation failure in IVF, and potential endometriosis. In men, although spermatogonial stem cells allow regeneration, pollutants impair sperm quality. Chronic exposure to heavy metals through contaminated water, cigarette smoke, and the food chain exacerbates epigenetic effects and fetal toxicity. Air pollution and heat stress also disrupt fertility by reducing oocyte and embryo production and lowering progesterone levels. This lecture emphasizes the need for public awareness and preventive measures, such as using high-efficiency air filters, reducing the use of BPA- and phthalate-containing plastics, and avoiding exposure to pollution sources, to safeguard reproductive health.

Inm-11: The Role of Midwives in Promoting Youth Population and Childbearing, with an Emphasis on Sexual and Reproductive Health

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In recent decades, Iran, like many other countries, has faced a trend of declining fertility rates, an increase in the age of marriage and childbearing, and, consequently, a growing aging population. These demographic shifts have led to multiple consequences in social, economic, and health dimensions, including a decrease in the young population, a rising need for care and health services, a reduction in the workforce, and challenges in maintaining economic dynamism and achieving sustainable development. The issue of a youthful population has now become a central concern for policymakers in Iran, leading to the implementation of numerous programs aimed at supporting childbearing and population growth. In this context, midwives, as key specialists in the field of reproductive health, play a crucial role in promoting sexual health, educating and supporting families, and facilitating informed decision-making about childbearing.

ing. A midwife's duties, beyond providing proper education on sexual and reproductive health to couples, include counseling on childbearing, preventing and identifying cases of infertility, collaborating in infertility treatment, especially in underserved areas, providing preconception care, addressing women's mental health, preventing abortion, and actively participating in the development and implementation of policies related to reproductive health. Furthermore, the specialized education provided by midwives leads to increased marital satisfaction, improved emotional interaction and relationships, awareness of mutual rights and duties, and ultimately, an increased inclination toward childbearing. From the perspective of national legal frameworks, the position of midwives in the country's population policies has been clearly defined. Higher-level policies, such as the General Population Policies and the Ministry of Health's regulations and guidelines, emphasize the role of midwives in education, counseling, and supporting women and families, especially mothers. The continuation and success of these population policies require a focus on midwifery and the increased support and empowerment of midwives within the healthcare system.

Inm-12: Genetic Factors in Male Infertility

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According to the World Health Organization's definition of infertility, couples who do not conceive after one year of unprotected sex are infertile. About 50 million couples worldwide suffer from infertility, and men are equally affected. Male infertility is a complex heterogeneous and multifactorial disorder. Like most diseases, genetic factors also play a role in this issue. Genetic defects such as Klinefelter syndrome (XXY), Y chromosome microdeletions (YCMDs), and single gene mutations are implicated in male infertility. Currently, 4% of infertile men have a genetic cause, while 60-70% remain undiagnosed. Trying to identify new genes/types that cause male fertility and then improving diagnostic panels are the goals of recent studies in this field. It is estimated that about 2000 genes are involved in the maintenance of germ cells and successful meiosis, while more than 100 genes have been identified in male infertility. Although karyotyping, Y chromosome screening, and microarray remain effective techniques for diagnosing male infertility, next-generation sequencing (NGS) is becoming a more widely used technique. NGS has accelerated the introduction of male infertility genes over the past decade and introduced more genes to infertility panels. The method hopes to reduce cases of unexplained male infertility and provide more information about them.

Inm-13: Genetics of Female Infertility: Current Status, Advances, and Future Directions

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Female infertility presents a significant clinical challenge, affecting reproductive health and quality of life. While environmental and hormonal factors are well-established contributors, genetic causes play a critical and often underrecognized role in many cases of female infertility. Recent advancements in genomic technologies, including next-generation sequencing and genome-wide association studies, have substantially deepened our understanding of the genetic basis of disorders such as premature ovarian insufficiency (POI), polycystic ovary syndrome (PCOS), endometriosis, and unexplained infertility. Identification of pathogenic variants in genes involved in ovarian development, folliculogenesis, meiosis, and hormonal regulation has provided new insights into the molecular mechanisms underlying impaired fertility. These findings hold promise for enhancing diagnostic precision and guiding personalized management strategies. However, significant challenges remain in translating genetic discoveries into routine clinical practice due to genetic heterogeneity, incomplete penetrance, and the complex interplay of genetic and environmental factors. This presentation will review the current status of genetic research in female infertility, discuss recent breakthroughs with clinical relevance, and explore future directions, including the integration of multi-omics data and advances in reproductive genetics counseling. The goal is to equip healthcare providers including physicians and geneticists with updated knowledge to improve patient care and foster collaborative approaches in managing female infertility.

Inm-14: The Necessity of Integrating Genetic Counseling into The Diagnosis and Treatment of Infertility

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Infertility, affecting an estimated 15% of couples worldwide, presents a complex clinical picture with far-reaching psychological and social consequences. Among the various contributing factors, genetic causes play a particularly important role—especially in cases of idiopathic infertility, recurrent pregnancy loss, and repeated failures of assisted reproductive technology (ART). Despite this, genetic counseling remains underutilized and is not yet routinely integrated into infertility treatment protocols in many fertility clinics across Iran. A comprehensive genetic assessment can significantly enhance the diagnostic process. In men, conditions such as Y chromosome microdeletions, Klinefelter syndrome, and CFTR mutations are key contributors to impaired spermatogenesis. In women, Turner syndrome, premature ovarian insufficiency, and pathogenic variants in genes involved in folliculogenesis are among the most commonly identified causes. The application of genetic testing -ranging from karyotype analysis and targeted gene panels to carrier screening and whole exome sequencing- can offer valuable insights, particularly for couples with a relevant family history or unexplained infertility. As ART becomes more widespread, the establishment of standardized clinical pathways that include timely referral to genetic counseling is essential. Integrating this service not only helps reduce the risk of transmitting hereditary conditions but also guides treatment selection and empowers couples to make informed reproductive decisions. Addressing the barriers to implementation -such as limited access, cost constraints, and lack of interdisciplinary

coordination- will be critical to expanding the role of genetic counseling in reproductive medicine throughout Iran.

Inm-15: Evaluation of Advanced Methods for Diagnosing Embryo Health

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Fetal genetic testing can be categorized into screening and diagnostic tests. Screening tests assess the risk of a fetus having certain genetic conditions, while diagnostic tests can confirm or rule out a specific genetic disorder. Key types include CVS, amniocentesis, and cell free DNA screening. Screening tests: First trimester screening, integrated or sequential screening, cf-DNA, quad screen. Diagnostic tests: CVS, Amniocentesis, PGT, PUBS.

Oral Speaker

Onm-1: Effect of Curcumin on Inflammatory Markers in Women with Polycystic Ovary Syndrome Undergoing Infertility Treatment

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Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder associated with various symptoms, including infertility. This study aims to investigate the impact of curcumin on inflammatory indicators in women with PCOS undergoing infertility treatment.

Materials and Methods: A randomized clinical trial was conducted on 60 infertile women with PCOS at Shahid Akbarabadi Hospital in Tehran. Participants were randomly assigned into curcumin and placebo groups and received either curcumin (500 mg three times a day) or a placebo for 6 weeks. Inflammatory markers were measured in blood and follicular fluid using commercially available kits. Data analysis was performed using SPSS 21 software.

Results: Curcumin consumption for 6 weeks led to a significant reduction in C-reactive protein ($P=0.025$), neutrophil to lymphocyte ratio ($P=0.036$), and body mass index ($P=0.039$). However, no significant changes were observed in interleukin-6 levels.

Conclusion: Daily consumption of 1500 mg of curcumin tablets for 6 weeks showed beneficial effects on inflammatory markers and body mass index in women with PCOS undergoing infertility treatment. Further studies are needed to confirm these findings in larger and longer-term trials.

Keywords: Curcumin, Turmeric, PCOS, Inflammation

Onm-2: The Effectiveness of Probiotics in the Fertility of Patients with Polycystic Ovary Syndrome who are Candidates for IVF

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Background: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age. Recent research has highlighted the role of gut microbiome in regulating metabolic and hormonal health. Gut microbiome dysbiosis is associated with increased systemic inflammation, insulin resistance, and hormonal disorders that can negatively affect ovarian function and egg quality. Probiotics may modulate the gut microbiome and improve metabolic and hormonal health in PCOS patients undergoing *in vitro* fertilization (IVF) treatment.

Materials and Methods: This randomized, double-blind clinical trial included 168 women with PCOS aged 18-35 years who were candidates for IVF. Participants were randomly divided

into probiotic ($n=84$) and control ($n=84$) groups. The intervention group received one oral probiotic capsule daily (LactoFem, 500mg containing 7 bacterial strains) for one month, followed by ovulation-stimulating drugs with continued probiotic supplementation in the second month. Primary outcomes were chemical and clinical pregnancy rates; secondary outcomes included number of punctured eggs and frozen embryos.

Results: The mean age was 29.01 ± 4.21 years. Chemical pregnancy rate was higher in the probiotic group compared to control (71.4% vs 56%; P value=0.038; OR=1.87, 95% CI [1.04-3.73]). Clinical pregnancy rate was also higher in the probiotic group (42.9% vs 32.1%; $P=0.153$; OR=1.58, 95% CI [0.84-2.97]). Probiotic supplementation resulted in 87% increased likelihood of chemical pregnancy and 67% decreased likelihood of ovarian hyperstimulation syndrome (OHSS).

Conclusion: Oral probiotic administration in women aged 18-35 with PCOS who are candidates for IVF significantly increased chemical pregnancy rates and reduced OHSS, suggesting probiotics may be a beneficial adjuvant therapy for improving fertility outcomes in this population.

Keywords: Polycystic Ovary Syndrome, Infertility, *In Vitro* Fertilization, Probiotics, Pregnancy Rate

Onm-3: Barriers to Reproductive Health in Female MS Patients and Their Husbands

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Background: Multiple sclerosis (MS) is a degenerative and progressive disease of the central nervous system. Reproductive health is one of the major factors strengthening the quality of life in patients. Therefore, we aimed to investigate how MS women and their husbands describe the MS symptoms on the worsening problems of reproductive health.

Materials and Methods: This qualitative study was done as part of a mixed-method study on 25 women with MS and their husbands in Iran MS Society. Purposive sampling and individual, semi structured interviews were used to gather qualitative data. Conventional content analysis approach was used to identify categories via MAXQDA 10 software.

Results: Results showed that issues and worries of reproductive health in multiple sclerosis women and their husbands consists of (1) urinary sexual dysfunction, (2) marital unsatisfaction, (3) maternal vulnerability, (4) limited contraception methods, and (5) social phobia. Each of these categories is included of codes and subcategories which conveyed the perception and experience of women about the reproductive health at the presence of multiple sclerosis.

Conclusion: The results of this study show that women with MS and their husbands are faced with concerns. These worries represent important factors that affect the health and function of reproductive system. Our findings showed that effective interventions by recognizing these factors should be performed to improve quality of life in MS patients especially those who have been recently diagnosed.

Keywords: Multiple Sclerosis, Qualitative Research, Reproductive Health

Onm-4: Assessment of The Dimensions and Prevalence of Stigma among Women in Shahrekord

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Background: Abortion, particularly in conservative societies, is often associated with significant social stigma that can adversely affect women's mental health, emotional well-being, and access to healthcare. This study aimed to examine the prevalence and key dimensions of abortion-related stigma among women in Shahrekord, Iran.

Materials and Methods: This descriptive cross-sectional study was conducted in 2025 in Shahrekord. A total of 110 women with a history of abortion who visited local healthcare centers were selected through convenience sampling. Data collection tools included a demographic questionnaire and a standardized abortion stigma scale. Data were analyzed using SPSS version 26. The study was approved by the Research Ethics Committee of Shahrekord University of Medical Sciences, and written informed consent was obtained from all participants.

Results: Findings indicated that 45% of participants experienced a high level of abortion-related stigma. The most frequently reported dimension was isolation, where many women felt unable to talk openly about their abortion or receive adequate emotional support. The second most prevalent dimension was fear of judgment, with participants expressing deep concern about disclosing their experience due to potential negative reactions. Social condemnation ranked third, reflecting experiences of blame or degrading treatment by others. The least reported dimension was self-judgment, suggesting that internal feelings of guilt or inadequacy were less prominent than external stigma. A significant association was found between the level of stigma and factors such as education level, marital status, and place of residence ($P < 0.05$).

Conclusion: The considerable prevalence of abortion-related stigma among women in Shahrekord highlights the urgent need for targeted psychosocial interventions and public education to reduce stigma and promote emotional support and social acceptance.

Keywords: Stigma, Abortion, Women

Poster Presentation

Pnm-1: The Effect of Apple Cider Vinegar on Anthropometric and Metabolic Parameters in Overweight and Obese Women with Polycystic Ovary Syndrome

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Background: Polycystic ovary syndrome (PCOS), a prevalent endocrine and metabolic disorder in reproductive-age women, is strongly associated with obesity, insulin resistance, and chronic low-grade inflammation. Given the increasing interest in natural interventions for weight management, apple cider vinegar (ACV) has emerged as a potential therapeutic agent. This review aimed to summarize the effects of ACV supplementation on anthropometric parameters and key metabolic profiles in overweight and obese women diagnosed with PCOS. **Materials and Methods:** A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science to examine the impact of ACV on inflammatory markers, insulin resistance, and obesity in PCOS patients. Only randomized controlled trials and clinical studies published between 2010–2023 were included.

Results: Daily consumption of ACV at all three doses (5, 10, and 15 ml) resulted in significant reductions in body weight, body mass index, waist/hip ratio, and body fat percentage compared to baseline values by week 12 ($P < 0.05$). Furthermore, significant improvements were observed in FBG, TG, and total cholesterol levels in the ACV groups. These beneficial effects appeared to be dose-dependent, with the 15 ml ACV group demonstrating the most pronounced improvements. No significant adverse effects were reported during the study period.

Conclusion: ACV supplementation effectively improves anthropometric measurements and metabolic markers in overweight and obese women with PCOS. These findings suggest that ACV may serve as a safe and promising complementary therapeutic strategy for managing obesity and its associated metabolic dysregulations in this patient population. Further research is warranted to confirm these effects and explore underlying mechanisms.

Keywords: Apple Cider Vinegar, Polycystic Ovary Syndrome, Obesity, Insulin Resistance, Metabolic Parameters

Pnm-2: The Effect of Apple Cider Vinegar on Hormonal Profiles, Insulin Sensitivity, and Ovulatory Function in Women with Polycystic Ovary Syndrome

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Background: Polycystic ovary syndrome (PCOS), a common endocrine disorder in reproductive-age women, is characterized by hyperandrogenism, ovulatory dysfunction, and metabolic disturbances, often leading to infertility. Given the limitations of current pharmacological treatments and the multifaceted nature of PCOS, exploring effective non-pharmacological interventions is crucial. This study evaluated apple cider vinegar's

(ACV) effects on hormonal balance, insulin sensitivity, and ovulation restoration in PCOS patients.

Materials and Methods: A structured literature search was conducted using PubMed, focusing on clinical studies (2010–2023) investigating ACV's impact on PCOS features (hirsutism, acne, menstrual irregularities, infertility). Both dietary and capsule-based ACV interventions were analyzed for hormonal and metabolic outcomes.

Results: Following ACV consumption, a notable improvement in insulin sensitivity was observed, with six out of seven patients (85.7%) exhibiting a decrease in HOMA-R. The LH/FSH ratio, a key hormonal marker in PCOS, decreased in five patients (71.4%). Significantly, ovulatory menstruation was restored within 40 days in four of the seven patients (57.1%) who were previously anovulatory.

Conclusion: These preliminary findings suggest that daily ACV consumption may improve insulin sensitivity and restore ovulatory function in women with PCOS. ACV could therefore represent a promising, accessible, and cost-effective complementary approach for managing key clinical manifestations of PCOS, particularly anovulation and insulin resistance. Further larger-scale, controlled clinical trials are warranted to confirm these benefits and elucidate underlying mechanisms.

Keywords: Apple Cider Vinegar, Polycystic Ovary Syndrome, Ovulatory Function, Hormonal Profile, Insulin Sensitivity

Pnm-3: Challenges and Opportunities of Artificial Intelligence Use in Infertility Nursing Care: A Systematic Review

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Background: With the rapid advancement of digital technologies, artificial intelligence (AI) is increasingly being integrated into healthcare services, particularly in the field of infertility. Infertility nursing, as a key component of assisted reproductive care, holds significant potential for AI integration. This review aims to identify the challenges and opportunities associated with implementing AI in infertility nursing care.

Materials and Methods: This structured systematic review was conducted by searching PubMed, Scopus, and Web of Science databases for articles published between 2022 and 2025. Keywords included "Artificial Intelligence," "Infertility Nursing," "Opportunities," and "Challenges." A total of 43 articles were retrieved, of which 18 met the inclusion criteria and were analyzed in detail.

Results: Key opportunities identified include enhanced infertility diagnosis through machine learning algorithms, personalized care planning, and improved nursing education using AI-powered simulations. Major challenges consist of patient distrust in algorithm-based decisions, ethical and legal concerns, and the lack of formal AI training among nurses.

Conclusion: Findings suggest that with appropriate investment in nurse education and the development of robust ethical and technical frameworks, AI can significantly improve the quality of infertility nursing care. Establishing international standards and guidelines is crucial for the safe and effective use of AI in this field.

Keywords: Artificial Intelligence, Infertility Nursing, Nursing Care, Health Technology, Ethical Challenges

Pnm-4: The Impact of Human Papillomavirus on Female Infertility: A Systematic Review

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Background: Infertility is defined as the inability to conceive after 12 months of regular, unprotected sexual intercourse. The human papillomavirus (HPV) is a non-enveloped, double-stranded, circular DNA virus that is responsible for causing multiple epithelial lesions and cancers and is the most common cause of sexually transmitted infections. It may affect the fertility of couples.

Materials and Methods: In this study, using the keywords infertility, HPV, and genital warts, a search was conducted in databases including Google Scholar, PubMed, SID, Web of Science, and ScienceDirect. A total of 33 articles from the years 2015–2025 were extracted, and 14 articles were selected based on the inclusion criteria.

Results: According to the findings, the causes of infertility related to HPV may be due to the immune response against the virus, the direct pathogenic effects of HPV, and its ability to cause DNA damage. Additionally, HPV infection may interfere with the migration of trophoblasts to the uterus, leading to infertility and recurrent miscarriages.

Conclusion: Considering national policies focused on population growth and childbearing, it is recommended to strengthen and expand educational foundations to raise awareness among couples about avoiding risky behaviors, prophylactic vaccination, and the symptoms and complications of HPV infection.

Keywords: Infertility, HPV, Genital Warts

Pnm-5: Artificial Intelligence in Infertility Diagnosis: Revolutionizing Detection and Treatment Strategies

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Background: This article explores how artificial intelligence (AI) is transforming the diagnosis and management of infertility. By leveraging machine learning, predictive modeling, and big data analytics, AI enhances accuracy in detecting infertility causes, personalizes treatment plans, and improves reproductive outcomes for both men and women.

Materials and Methods: A systematic review was conducted using studies from PubMed, Scopus, and IEEE Xplore databases. Keywords included "AI in infertility," "machine learning for fertility diagnosis," "predictive modeling in reproductive medicine," and "automated semen analysis." Studies published up to 2024 were analyzed to assess AI's role in improving diagnostic precision, reducing human error, and optimizing fertility treatments.

Results: AI applications in infertility diagnosis show significant promise: • Semen Analysis: AI-powered systems (e.g., automated sperm morphology assessment) outperform manual

methods in speed and accuracy. • Ovarian Reserve & Follicle Tracking: Deep learning models predict ovarian response to stimulation in *in vitro* fertilization (IVF) with high reliability. • Endometrial Receptivity: AI algorithms analyze ultrasound and hormonal data to determine optimal embryo implantation timing. • Male & Female Factor Infertility: Predictive models integrate genetic, hormonal, and lifestyle data to identify underlying causes. Challenges include data privacy concerns and the need for large, diverse datasets to train robust AI models.

Conclusion: AI is reshaping infertility diagnosis by enabling faster, more precise, and personalized care. Continued advancements in machine learning, coupled with interdisciplinary collaboration, will further enhance reproductive medicine. Wider adoption of AI tools in clinics can improve success rates and reduce the emotional and financial burden of infertility treatments.

Keywords: Artificial Intelligence, Infertility Diagnosis, Machine Learning, IVF Optimization, Automated Semen Analysis

Pnm-6: Harnessing Artificial Intelligence to Revolutionize Infertility Diagnosis: Advances and Future Directions

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Background: Infertility affects a significant proportion of couples worldwide, with complex etiologies that pose diagnostic challenges. Traditional assessment methods are often time-consuming and subject to inter-observer variability. Recent advances in artificial intelligence (AI) offer promising solutions to enhance diagnostic accuracy, efficiency, and personalized treatment planning in infertility evaluation.

Materials and Methods: This review synthesizes current literature on AI-driven technologies employed in infertility diagnosis, including machine learning algorithms, deep learning models, and image analysis tools. Data were collected from peer-reviewed journals, clinical trials, and technological reports published up to October 2023. The study analyzes AI applications in semen analysis, embryo assessment, ultrasound imaging, hormonal profiling, and predictive modeling.

Results: AI-based systems have demonstrated superior accuracy in sperm morphology and motility analysis, reducing observer bias. Deep learning models applied to ultrasound and 3D imaging improve embryo quality assessment and endometrial receptivity prediction. Machine learning algorithms integrating hormonal, genetic, and imaging data enhance the predictive accuracy of fertility outcomes. These innovations have led to faster diagnostics, improved treatment personalization, and better success rates in assisted reproductive technologies.

Conclusion: AI is transforming infertility diagnostics by providing more precise, efficient, and reproducible assessments. Continued development and integration of AI technologies hold great promise for personalized medicine approaches, optimizing outcomes in reproductive health. Future research should focus on large-scale validation, ethical considerations, and integrating AI tools into clinical workflows to fully realize their potential.

Keywords: Artificial Intelligence, Revolutionize, Infertility, Future Directions

Pnm-7: The Role of AI-Driven Technologies in Improving

Accuracy and Efficiency in Infertility Assessment

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Background: Infertility affects approximately 10-15% of couples worldwide and presents significant emotional, social, and financial challenges. Traditional assessment methods involve a combination of patient history, hormonal profiling, imaging studies, and invasive procedures, which can be time-consuming and sometimes limited in accuracy. Recent advancements in Artificial Intelligence (AI), particularly machine learning and deep learning, offer promising solutions to address these limitations. AI's capacity to analyze complex datasets, automate image interpretation, and predict treatment responses has the potential to revolutionize infertility diagnostics, making assessments more accurate, efficient, and personalized.

Materials and Methods: This review synthesizes data from peer-reviewed articles, clinical trials, and systematic reviews published between 2018 and 2023. Databases such as PubMed, Scopus, and IEEE Xplore were searched using keywords like "AI in infertility," "machine learning reproductive health," and "AI diagnostic tools in fertility." Selected studies included those evaluating AI applications in ultrasound imaging, hormonal analysis, embryo selection, and treatment outcome prediction. Data extraction focused on the accuracy, efficiency, and clinical impact of AI technologies. Comparative analysis was conducted to assess AI performance against conventional diagnostic methods.

Results: The analysis revealed that AI algorithms significantly enhance the interpretation of ultrasound images, leading to more accurate identification of ovarian and uterine abnormalities. In embryo selection, AI models outperformed traditional grading systems by predicting implantation success with higher precision. Machine learning-based prediction models demonstrated improved accuracy in forecasting treatment outcomes, such as response to ovulation induction and IVF success rates. Furthermore, AI-powered tools reduced diagnostic timeframes and minimized human error, contributing to more efficient clinical workflows. Challenges identified include the need for large, diverse datasets to improve model generalizability and integration into existing clinical practices.

Conclusion: AI-driven technologies hold substantial promise in transforming infertility assessment by increasing diagnostic accuracy and operational efficiency. Their application facilitates personalized treatment plans and may improve reproductive success rates. Future research should focus on larger, multi-center studies to validate AI models and on developing user-friendly interfaces for seamless clinical integration. Embracing AI in reproductive medicine can ultimately lead to more effective and patient-centered infertility care.

Keywords: Efficiency in Infertility, AI-Driven Technologies, Transforming Infertility

Pnm-8: Barriers and Facilitators of Acceptance of Infertility Treatment: A Systematic Review

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Background: Infertility significantly affects couples' physical, psychological and social health, with women disproportionately impacted. Although ART has advanced, treatment acceptance remains challenging. This systematic review identifies barriers and facilitators to treatment adoption, providing evidence to help clinicians develop targeted interventions that improve patient engagement.

Materials and Methods: This systematic review conducted a comprehensive search across PubMed, ProQuest, Scopus, Web of Science, Cochrane Library, Magiran, SID, and Google Scholar for English and Persian articles published between 2000 and 2025. Keywords included MeSH terms such as "Infertility," "Subfertility," "Treatment seeking," "Health-seeking behaviors," and "Patient acceptance of treatment," combined with Boolean operators (AND/OR). Inclusion criteria encompassed qualitative, quantitative, and mixed-methods studies addressing infertility treatment acceptance. Data extraction and synthesis adhered to PRISMA guidelines, utilizing qualitative and content analysis to evaluate findings.

Results: The review identified 31 eligible studies from 4426 articles. Key barriers to treatment acceptance were high treatment costs, physical/psychological side effect concerns, fear of failure, social stigma or judgment, cultural/religious beliefs, lack of treatment awareness, and insufficient spousal or family support. On the other hand, facilitators included partner-supported parenthood desire, healthcare provider education, health literacy, easy access to treatment centers, strong social support, peer positive experiences (by friends or acquaintances), and insurance coverage.

Conclusion: This systematic review highlights that infertility treatment acceptance is shaped by individual, social, and systemic factors. Integrating these factors into care, counseling, and education programs led by midwives and nurses can enhance treatment outcomes and alleviate psychological burdens on couples. The study advocates for infertility treatment teams to prioritize a holistic, patient-centered approach.

Keywords: Infertility, Treatment Seeking, Health-Seeking Behaviors, Patient Acceptance of Treatment, Systematic Review

Pnm-9: The Relationship between Persistent Organic Pollutants and Ovarian Reserve: A Systematic Review

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Background: Persistent organic pollutants (POPs) are industrial chemicals resistant to degradation and have adverse effects on reproductive health in wildlife and humans. Despite regulations reducing their levels, POPs remain widespread and pose a global concern. These chemicals are linked to reduced fertility in women, which depends heavily on the ovarian reserve—a prenatally determined stock of non-growing follicles essential for reproductive capacity. Assessing the impact of POP exposure on women's fecundity is challenging but necessary. This systematic review investigated associations between chemical exposures and ovarian reserve.

Materials and Methods: In this systematic review, databases including PubMed, Web of Science, Scopus, ProQuest, and Google Scholar were searched using the keywords "Ovarian

reserve", "Persistent organic pollutants", "Infertility", and their English equivalents with the help of Boolean operators OR and AND. All observational studies from 2010 to the end of 2025 were included. There were no restrictions on the language of publication of the articles.

Results: Eight relevant articles were selected for detailed evaluation. Findings showed that hexachlorobenzene (HCB), transnonachlor, and polychlorinated biphenyls (PCBs 74 and 99) were associated with decreased non-growing follicle densities. HCB and transnonachlor also correlated negatively with healthy follicle density. Mixtures of lipophilic POPs—including PBDE 99, p,p'-DDE, and PCB 187—were linked to lower non-growing follicle densities. Additionally, higher levels of PCB congeners were inversely associated with ovarian reserve markers such as antral follicle count and follicular response to gonadotropins (peak estradiol, number of oocytes retrieved, endometrial thickness).

Conclusion: This systematic review confirms that POPs negatively affect female fertility. Although many POPs are no longer produced, their persistence results in continued detection in human biological samples. Therefore, reducing exposure and re-considering the use and production of POPs should be a priority for governments globally

Keywords: Ovarian Reserve, Persistent Organic Pollutants, Infertility

Pnm-10: Fear of Infertility Experiences: A Conflict in Concerns of Women with Multiple Sclerosis

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Background: Little is known about fertility experiences and concerns of women with multiple sclerosis (MS) in Iran, where a relatively high prevalence of MS, especially among reproductive-age women, is observed.

Materials and Methods: This qualitative study explored the fertility experiences and concerns of women who were diagnosed with MS. Semi-structured and face-to-face interviews were conducted with twenty-five women with MS. Recorded and transcribed interviews were analyzed using a content analysis approach through MAXQDA.10 software.

Results: Disrupted menstruation, worrying about the effects of MS, and limited infertility treatments caused by MS, led to fear about infertility. The participants expressed that they were afraid of becoming pregnant and having babies due to the complications of MS. They also referred to their fertility, which is being threatened by MS, and were worried they might not be able to become mothers in the future. This can be a conflict in the concerns of women with MS. However, these women received little support for their fertility.

Conclusion: This study increased our understanding of how women's experiences of MS create a conflict between their concerns about fertility. This conflict could interfere with their decision-making and cause them to miss the opportunities and golden time for becoming a mother. Therefore, awareness, education, and support should be extended among women with MS, their spouses, and families, from early stages after the MS diagnosis.

Keywords: Multiple Sclerosis, Fertility, Concerns, Conflict

Pnm-11: Polycystic Ovary Syndrome and Metabolic Syndrome: A Global Perspective

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Background: Polycystic ovary syndrome (PCOS) affects 8-13% of reproductive-aged women and is characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology. Its strong association with metabolic syndrome (MetS) -marked by insulin resistance, dyslipidemia, and obesity- significantly increases cardiovascular risk. This review examines global evidence on biomarkers, metabolic risks, and management strategies for PCOS-related MetS.

Materials and Methods: A systematic review (2015-2025) analyzed 32 studies from multiple countries (China, Iran, Brazil, Poland, Nepal, Korea) following PRISMA/STROBE guidelines. Included were 819 PCOS women, 3,122 controls, and 315 adolescents, diagnosed via Rotterdam criteria (or adolescent-specific guidelines). MetS was defined by NCEP/ATP III or IDF standards. Key assessments included metabolic markers (AMH, TyG index, ApoB/ApoA1), hormonal profiles, and psychological screening (CESD-R). Statistical analysis used logistic regression and ROC curves (SPSS, $P < 0.05$).

Results: MetS prevalence in PCOS was 32.5–59.3% (vs. 9.2% in controls, $p = 0.01$), with a 4-fold increased risk (OR: 4.14). Key features included low HDL-C (84.9%) and central obesity (56.6%). Biomarkers like AMH (13.92 ng/mL in Phenotype 1), TyG index (cutoff: 8.65), and ApoB/ApoA1 (AUC: 0.84) showed strong diagnostic value. Hyperandrogenic phenotypes and 25.1% of adolescents exhibited elevated HOMA-IR. Depression (33.0%) further increased MetS risk (aHR: 1.56, $P = 0.01$). Low zinc/selenium intake correlated with worse outcomes.

Conclusion: PCOS markedly elevates MetS risk, underscoring the need for early biomarker screening (AMH, TyG) and targeted interventions. Adolescents and hyperandrogenic subgroups require close monitoring. Integrating depression screening and nutritional strategies (zinc, myo-inositol) is essential. Future research should validate biomarkers and explore microbiota interactions for personalized care.

Keywords: Polycystic Ovary Syndrome, Metabolic Syndrome, Insulin Resistance, Biomarkers, Personalized Medicine

Pnm-12: The Connection between Chronic Pelvic Pain and Endometriosis: A Literature Review

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Background: Endometriosis, affecting 6-10% of reproductive-age women, is a major cause of chronic pelvic pain (CPP) and infertility. CPP, defined as persistent pelvic pain lasting over six months, significantly impacts quality of life. The pain arises from inflammation, estrogen dependence, and neurogenic mechanisms, leading to dysmenorrhea, dyspareunia, and central sensitization. This review examines the pathophysiology, diagnosis, and management of endometriosis-associated CPP.

Materials and Methods: A systematic search was conducted in PubMed, Google Scholar, and Scopus (2015-2025), identifying 26 relevant studies. Included were women aged 18-45 with CPP and surgically confirmed endometriosis (laparoscopy, MRI, or ultrasound). Exclusions were fibroids, pelvic inflammatory disease, or recent hormonal therapy. Data extraction covered pain assessment (Visual Analogue Scale), cytokine levels, and treatment outcomes (antioxidants, acupuncture, nerve blocks).

Results: Endometriosis-related CPP involves elevated pro-inflammatory cytokines (IL-6, IL-8, TNF- α) and oxidative stress markers. Antioxidant supplementation (vitamins C, E, D) reduced pain and inflammation. Acupuncture and hypogastric plexus blocks showed efficacy in pain relief. Laparoscopic excision confirmed endometriosis in 73% of CPP cases and significantly decreased pain severity.

Conclusion: Endometriosis contributes to CPP through inflammatory, hormonal, and neuroplastic mechanisms. While antioxidants and interventional therapies offer promising results, further research is needed on personalized treatment strategies, including microbiome modulation and neuropathic pain management.

Keywords: Endometriosis, Chronic Pelvic Pain, Inflammation, Central Sensitization, Antioxidant Therapy

Pnm-13: Hope and Innovation in Fertility Care for Women with Premature Ovarian Insufficiency (POI): A Review of Current and Emerging Strategies

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Background: Premature ovarian insufficiency (POI) affects around 1% of women under 40 and can have a life-changing impact, particularly for those who hope to have children. This review brings together recent research on the causes of POI and the promising new treatments that may help women preserve or even restore fertility.

Materials and Methods: We reviewed ten high-quality articles from respected journals indexed in PubMed, Scopus, and Web of Science. These studies covered a range of topics -from the biological roots of POI (such as genetics, autoimmunity, and oxidative stress) to treatment options like hormone therapy, ovarian tissue freezing, in vitro activation (IVA), and stem cell therapies.

Results: POI can be caused by a mix of factors, including inherited conditions like Turner syndrome and Fragile X, autoimmune issues, or damage from cancer treatments like chemotherapy. Some cases remain unexplained. New research highlights the role of oxidative stress and inflammation in speeding up ovarian aging. Excitingly, newer therapies -like activating dormant follicles in the lab (IVA) or transplanting stem cells from umbilical cords- have shown potential to revive ovarian activity and hormone function. Meanwhile, hormone replacement therapy continues to be essential for managing symptoms and protecting long-term health, and fertility preservation techniques are now more accessible for at-risk patients.

Conclusion: While POI presents a significant challenge, science is catching up with hope. By better understanding the many faces of this condition, clinicians can now offer more personalized support. New technologies are opening doors to once unimaginable fertility options. However, more clinical tri-

als are needed to confirm the safety and success of these novel treatments.

Keywords: Premature Ovarian Insufficiency, Fertility, Ovarian Aging, Oxidative Stress, *In Vitro* Activation

Pnm-14: How Artificial Intelligence Is Changing Infertility Diagnosis and Treatment

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Background: This review looks at how artificial intelligence (AI) is helping doctors better diagnose and treat infertility, with the goal of improving chances for couples trying to conceive.

Materials and Methods: We searched databases like PubMed, Scopus, and ISI Web of Science for studies published up to 2024. The keywords we used included "artificial intelligence," "infertility," "machine learning," "predictive models," and "reproductive medicine." We focused on studies that showed how AI tools analyze reproductive data, predict fertility success, or assist in clinical decision-making. We summarized the findings to see how effective and accurate these new approaches are.

Results: The studies show that AI algorithms, especially machine learning, can analyze complicated reproductive data -such as semen quality, embryo images, and hormone levels- with high accuracy. These tools often outperform traditional methods and help predict *in vitro* fertilization (IVF) success more reliably. They also assist in choosing the best embryos for transfer, which can improve the chances of pregnancy. In addition, AI models are useful in counseling couples about their fertility outlook and tailoring personalized treatment plans, reducing unnecessary procedures.

Conclusion: AI has huge potential to make infertility diagnosis and treatment more precise and personalized. By helping clinicians make smarter decisions, AI could increase success rates for fertility treatments like IVF. Still, we need more large-scale studies and careful ethical considerations to ensure these tools are safe, ethical, and widely accessible in everyday clinical practice.

Keywords: Artificial Intelligence, Infertility, Machine Learning, Embryo Selection, Reproductive Health

Pnm-15: Fertility and Sleep Disorders: Exploring The Interconnected Pathways in Women's Reproductive Health

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Background: While sleep is essential to overall health, its impact on fertility has only recently started to receive the attention it deserves. This presentation explores how sleep disturbances -such as short sleep duration, insomnia, and poor sleep quality- may affect fertility outcomes in women. It also examines the potential role of melatonin as both a sleep aid and a fertility-supportive supplement.

Materials and Methods: We reviewed evidence from recent clinical trials and observational studies involving over 2,500 women undergoing fertility evaluation or treatment. These in-

cluded women diagnosed with conditions like polycystic ovary syndrome (PCOS), endometriosis, and unexplained infertility (UI). Studies analyzed included those by Eisenberg et al. (2021), Esmaeilzadeh et al. (2025), Espino et al. (2019), and others. The focus was on sleep patterns, psychological stress, melatonin supplementation, and reproductive outcomes such as oocyte quality, pregnancy, and live birth rates.

Results: Sleep disturbances were significantly more common in women with PCOS and UI -particularly snoring, short sleep (<6 hours), and daytime fatigue. These were often linked with insulin resistance and mood issues. Melatonin, a natural sleep hormone with antioxidant properties, improved sleep and reduced pain in women with endometriosis, and showed promising results in improving oocyte quality and embryo development in IVF patients. Stress and poor sleep were also shown to reduce quality of life during fertility treatment and may indirectly impact outcomes.

Conclusion: Sleep is more than just rest -it's deeply tied to hormonal balance, mental health, and reproductive success. Melatonin supplementation may offer a simple, low-risk way to improve both sleep and fertility potential. Addressing sleep and stress as part of fertility care could lead to better experiences and outcomes for patients.

Keywords: Sleep, Infertility, Melatonin, PCOS, Endometriosis

Pnm-16: Lifestyle Modifications and Environmental Factors in Preventing Infertility

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Background: Infertility is a significant public health issue that affects many couples globally. It is influenced by a variety of factors, including lifestyle, chronic diseases, environmental exposures, and genetic predispositions. Identifying and preventing the risk factors contributing to infertility is essential for improving reproductive health and reducing the incidence of infertility. This study systematically reviews the factors contributing to infertility and preventive measures that can be taken to mitigate them.

Materials and Methods: This research was conducted using a systematic review approach. Data were collected from reputable databases, including Scopus, PubMed, and Web of Science, focusing on articles published between 2010 and 2024. The studies selected were based on PRISMA guidelines to ensure rigorous selection and data analysis processes.

Results: The results of the study indicate that multiple factors contribute to infertility, including hormonal imbalances, chronic diseases such as diabetes and thyroid disorders, obesity, smoking, alcohol consumption, chronic stress, and environmental pollutants. Additionally, lifestyle changes, such as weight management, dietary adjustments, smoking and alcohol cessation, and stress management, were found to have a significant impact on the prevention of infertility.

Conclusion: Preventive interventions, including lifestyle modifications, preconception screening, and counseling for couples, play a crucial role in reducing infertility prevalence. Furthermore, the establishment of comprehensive educational programs and public health policies aimed at raising awareness and improving access to preventive infertility services could serve as an effective strategy to mitigate the problem.

Keywords: Infertility, Healthy Lifestyle, Reproductive Health

Pnm-17: The Effect of Nonalcoholic Fatty Liver Disease on Sexually Diseases and Infertility

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Background: Nonalcoholic fatty liver disease is considered a hallmark of metabolic syndrome and a major risk factor for cardiovascular disease. The strong association between metabolic syndrome and male sexual dysfunction is now well established. Recent animal and human studies have further evaluated the association of nonalcoholic fatty liver disease with male sexual dysfunction and infertility. Therefore, the present study was conducted with the aim of reviewing the effectiveness of Non-alcoholic fatty liver disease on sexual disorders and infertility.

Materials and Methods: Academic and step-by-step search according to the purpose of study of PubMed, Googol Scholar, SID, and Magiran were investigated during the years 2020-2025. Then the articles were selected based on the inclusion criteria. Articles published in English and Persian with the same research topic and purpose they started studying. Studies that specifically discussed theories or case reports, or quality were included in the exit qualities.

Results: Sexuality is a central aspect of human life and is significantly affected by chronic diseases. Cirrhosis serves as a case in point, due to its unique pathophysiology and side effects of common treatments and is associated with very high rates of sexual and reproductive dysfunction in both men and women. Adequate control of underlying liver disease and factors causing sexual dysfunction is essential. All patients with liver disease and cirrhosis should be evaluated, as sexual dysfunction is amenable to correction and treatment, leading to improved quality of life.

Conclusion: Sexual dysfunction in liver disease is one of the most neglected health issues, and more prospective studies are needed on this potentially treatable topic.

Keywords: Nonalcoholic Fatty Liver Disease, Sexual Disorders, Infertility

Pnm-18: Application of Nanoparticles in IVF

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Background: With significant advancements in nanotechnology, nanoparticles have become one of the most important tools in medicine. In the field of infertility and *in vitro* fertilization (IVF), nanoparticles can play a crucial role in improving the quality of oocytes, sperm, and the culture environment of embryos. This paper explores the applications of nanoparticles in IVF processes and their effects on the therapeutic outcomes of IVF treatments.

Materials and Methods: This study was conducted using a systematic review approach. Articles related to the use of nanoparticles in IVF were retrieved from reputable databases such as Scopus, PubMed, and Web of Science. Published papers

between 2010 and 2024 were selected and analyzed. Various synthesis methods of nanoparticles and their impacts on IVF outcomes were examined.

Results: The findings indicate that nanoparticles are utilized in IVF for various purposes, such as enhancing fertility, protecting oocytes and sperm from oxidative damage, facilitating fertilization, and improving embryo culture environments. Metallic and polymeric nanoparticles, particularly gold, silver, and iron oxide nanoparticles, have shown positive effects on gamete quality and embryo development.

Conclusion: The application of nanoparticles in IVF has the potential to increase therapeutic success rates, improve fertilization rates, reduce oxidative damage, and enhance the transfer of higher-quality embryos. However, challenges such as nanoparticle toxicity, the need for further research to assess long-term safety, and the standardization of nanoparticle applications in IVF remain significant issues.

Keywords: Nanoparticles, Oocyte Quality, Infertility, IVF

Pnm-19: The Role of Artificial Intelligence in Enhancing Patient-Centered Healthcare: A Systematic Review

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Background: The rapid advancement of emerging technologies, particularly Artificial Intelligence (AI), has created unprecedented opportunities to enhance the quality of healthcare services. Patient-centered care, which prioritizes patients' needs, preferences, and values, stands to benefit significantly from integration with AI-driven systems. This study aims to explore the applications of AI in optimizing patient-centered healthcare.

Materials and Methods: A systematic review methodology was employed. Relevant literature was retrieved from the Scopus, PubMed, and Web of Science databases. Articles published between 2015 and 2024 that examined the role of AI in enhancing patient-centered care were selected. The article selection and data analysis processes followed PRISMA guidelines.

Results: The findings indicate that AI technologies -particularly machine learning, natural language processing, and recommendation systems- play a crucial role in advancing various aspects of healthcare, including early diagnosis, accurate clinical decision-making, personalized intervention design, and improved patient experiences.

Conclusion: AI demonstrates significant potential to improve clinical outcomes, enhance the quality of healthcare services, and increase patient satisfaction. Nonetheless, important challenges such as data privacy protection, algorithmic bias mitigation, and ethical considerations must be addressed. Establishing comprehensive legal and ethical frameworks and empowering healthcare professionals are essential to fully leveraging AI in patient-centered care.

Keywords: Artificial Intelligence, Patient-Centered Care, Digital Health, Personalized Medicine

Pnm-20: Genetic Disorders and Their Impact on Infertility: Diagnosis and Treatment Approaches

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Background: Infertility is a prevalent condition with various underlying causes, including genetic factors. Genetic disorders can significantly impact both male and female fertility, leading to challenges in conception and reproductive health. This study aims to explore the role of genetic diseases in infertility and their implications for diagnosis and treatment.

Materials and Methods: A systematic review was conducted by analyzing studies published between 2010 and 2024 from reputable databases, including Scopus, PubMed, and Web of Science. The selected articles focused on genetic disorders associated with infertility and the diagnostic and therapeutic approaches to manage these conditions.

Results: Several genetic disorders are linked to infertility, including: 1. Turner Syndrome: This chromosomal disorder, caused by the complete or partial absence of one X chromosome, leads to ovarian failure and infertility in females. Women with Turner syndrome typically experience impaired oocyte development and cannot conceive naturally. 2. Patau Syndrome (Trisomy 13): Patau syndrome, caused by an extra copy of chromosome 13, results in severe developmental and reproductive issues. This disorder can lead to recurrent miscarriages and challenges in pregnancy, further complicating fertility. 3. Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Mutations: Mutations in the CFTR gene, responsible for cystic fibrosis, cause male infertility due to obstructive azoospermia, while in females, it may lead to issues with ovulation and fertilization. 4. Chromosomal Abnormalities: Various chromosomal abnormalities, such as trisomies and structural chromosomal rearrangements, can contribute to infertility by disrupting normal gametogenesis and embryo development.

Conclusion: Early genetic testing, including preimplantation genetic testing (PGT) and intracytoplasmic sperm injection (ICSI), plays a critical role in diagnosing genetic causes of infertility. These approaches can improve the chances of successful pregnancies in patients with genetic disorders. However, challenges such as the excessive cost of testing, ethical considerations, and long-term safety require further investigation.

Keywords: Genetics, Chromosomal Abnormalities, Infertility, ICSI, PGT

Pnm-21: The Association between Stress, Anxiety, and Depression with Sexual Function of Women with Ovarian Insufficiency in the West of Iran: A Cross-sectional Study

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Background: Given the prevalence of ovarian insufficiency in the community and the limited number of studies on the impact of psychological factors on the sexual health of affected women, this study aimed to investigate the association between stress, anxiety, and depression and sexual function in women with ovarian insufficiency in western Iran.

Materials and Methods: This cross-sectional study was conducted on 240 women between January and April 2025. Participants included women with ovarian insufficiency undergoing infertility treatment at the Fatemeh Infertility Center, a referral hospital in Hamadan, Iran. Data collection tools included a demographic and laboratory information form, the short form of the depression, anxiety, and stress scale (DASS-21), and the female sexual function index (FSFI) questionnaire. Statistical analyses were performed using Stata software (version 14; StataCorp LLC, College Station, TX, USA), with a significance level of 0.05.

Results: Depression, anxiety, and stress exhibit strong inter-correlations (0.48–0.57) and robust inverse correlations with all sexual function domains (negative correlations up to -0.65). Components of the FSFI questionnaire (e.g., desire, arousal, satisfaction) demonstrate high correlations (0.57–0.85). In addition, among the categorical variables analyzed, only economic status (mean FSFI score: 14.55 for poor vs. 15.87 for intermediate, $P=0.02$) and family history of infertility (mean FSFI: 14.24 with history vs. 15.86 without, $P=0.009$) show statistically significant associations with total sexual function. The analysis of total mental health scores across categorical variables revealed that family history of infertility showed a statistically significant association ($P=0.009$), with individuals reporting a family history scoring higher (Mean=47.94, SD=5.68) compared to those without (Mean=45.15, SD=6.87).

Conclusion: Depression, anxiety, and stress robust inverse correlations with all sexual function domains. Economic status and family history of infertility show statistically significant associations with total sexual function. Family history of infertility showed a statistically significant association with total mental health scores. Finding is recommended that psychological counseling classes be offered to women with ovarian insufficiency.

Keywords: Ovarian Insufficiency, Stress, Anxiety, Depression

Pnm-22: Study of Reproductive Health Screening Methods in Patients with Poor Ovarian Response

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Background: Reduced ovarian reserve can manifest as a decrease in the quality or quantity of eggs or fertility potential, and no single screening method has yet been approved for this assessment. Therefore, the present study aimed to investigate reproductive health screening methods in patients with poor ovarian response.

Materials and Methods: The study reviewed several significant articles in the field between 2010 and 2024. Reviews in the journal and PubMed, Science Direct, Elsevier, ProQuest, Wiley, Springer, and google scholar databases with keywords Infertility, poor ovarian response, Reproductive health, screening. The results were analyzed and ranked schematically. For statistical analysis, statistical tests were used.

Result: Reproductive health screening in patients with poor

ovarian response includes tests performed to assess ovarian function, egg reserve, and ovarian response to assisted reproductive treatments such as in vitro fertilization. These tests include hormone levels (FSH, LH, AMH, estradiol), antral follicle count, and clomiphene challenge testing. These tests should be performed in high-risk women, including those aged 35 and over, those with a family history of premature menopause (ovarian failure), women who smoke, women who have unexplained infertility, women with autoimmune diseases, pelvic infections, women with a history of severe endometriosis, chemotherapy, radiation therapy, or previous surgery on the ovaries, and women who follow a vegetarian diet. It should be noted that there is a lot of evidence that performing these tests in low-risk groups leads to an increase in false positives of these tests. In vegetarian diets, in animal models, low-protein diets have been shown to have adverse effects on fertilization rates, ovarian follicle counts, and ovarian reserve in vegetarian women. This is more common in vegans (a diet that excludes or excludes animal products, including dairy and eggs) than in non-vegetarians.

Conclusions: The results of the present study showed that, considering the effects of premature ovarian failure on people's lives, it is better to recommend and implement reproductive health considerations and screenings before the onset of symptoms.

Keywords: Infertility, Reproductive Health, Poor Ovarian Response, Screening

Pnm-23: Considerations and Screenings for Reproductive Health in Women with Poor Ovarian Response

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Background: One of the biggest challenges in infertility medicine is the evaluation and treatment of patients with poor ovarian response (POR). A poor response to ovarian stimulation is a reproductive disorder that leads to infertility. Therefore, it is important to pay attention to reproductive health screenings in these women. Therefore, the present review study was conducted to investigate reproductive health screening in women with POR.

Materials and Methods: The study reviewed several significant articles in the field between 2010 and 2024. Reviews in the journal and PubMed, Science Direct, Elsevier, ProQuest, Wiley, Springer, and Google Scholar databases with keywords Infertility, poor ovarian response, Reproductive health, and screening. The results were analyzed and ranked schematically. For statistical analysis, statistical tests were used.

Results: The findings of the study showed that most of the symptoms of this disease appear due to the decrease in estrogen. Its symptoms are similar to those of menopause. Its most important symptoms include amenorrhea, reduced chance of pregnancy, infertility, reduced or non-responsiveness to fertility treatments, early onset of menopausal symptoms such as hot flashes, and increased risk of miscarriage. Therefore, considerations and screenings for reproductive health that we consider include: hormone therapy to prevent osteoporosis and reduce menopausal symptoms such as hot flashes, calcium and vitamin D intake to prevent osteoporosis, treatment of infertility and rosacea and egg storage, rich diet From calcium, training

and counseling for having children and not having a contraceptive method, doing weight bearing sports such as walking and strength training. Also, in the field of traditional medicine, the use of coriander syrup, oregano and chamomile decoction, and marshmallow plant; Rose and cheese are recommended.

Conclusions: The results of the present study showed that considering the effects of POR on people's lives, it is better to recommend and implement reproductive health considerations and screenings for all people before the onset of symptoms and even during treatment.

Keywords: Infertility, Reproductive Health, Poor Ovarian Response, Screening

Pnm-24: Association between Maternal ABO Blood Group and Recurrent Preterm Delivery: Evidence from A Cross-Sectional study

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Background: ABO blood groups have been associated with an increased risk of certain pregnancy complications. Conflicting results exist regarding the relationship between maternal ABO blood groups and preterm delivery. This study aimed to investigate the association between maternal ABO blood group and the recurrence of preterm delivery.

Materials and Methods: This cross-sectional study included 3763 pregnant women referred to Shahid Mostafa Khomeini Maternity Hospital in Ilam, Iran. Data were collected using a researcher-developed questionnaire comprising 37 items on individual, obstetric, and medical history, as well as fetal variables (gestational age, previous deliveries, birth weight, Apgar score, perinatal mortality, congenital anomalies, history of prior preterm delivery, presentation, placental disorders, history of abortion, history of hypertension, gestational diabetes, history of trauma or surgery, history of infertility, blood group, uterine and cervical structural abnormalities, and premature rupture of membranes). Data analysis was performed using SPSS Version 21 with chi-square and t-tests. A p value <0.05 was considered statistically significant.

Results: Among 350 cases of preterm delivery, 289 (82.6%) had no history of prior preterm delivery, while 61 (17.4%) had a history of previous preterm delivery. In the recurrent preterm delivery group, 20 (32.8%) had a gestational age less than 34 weeks, compared to 106 (36.7%) in the preterm delivery group (p value=0.072). Blood group O was the most frequent in both the recurrent preterm delivery group (23, 34.4%) and the preterm delivery group (129, 34.6%), while blood group A was the least frequent (recurrent preterm delivery: 11, 18.1%; preterm delivery: 48, 16.6%). The two groups showed a statistically significant difference in blood group distribution (P=0.04).

Conclusion: Based on the findings of this study, blood group O is significantly associated with preterm delivery.

Keywords: Preterm Delivery, Blood Group, Recurrent Preterm Delivery

Pnm-25: The Impact of Infertility History on Recurrent

Preterm Birth before 34 Weeks: Evidence from a Cross-Sectional study

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Background: Recurrent preterm birth (PTB) before 34 weeks poses significant maternal and neonatal risks. Emerging evidence suggests infertility history may exacerbate this risk, yet its role remains underexplored in populations with high PTB rates. This study evaluates the association between infertility history and recurrent PTB before 34 weeks in a high-risk population.

Materials and Methods: This cross-sectional study included 3,763 pregnant women attending Shahid Mostafa Khomeini Hospital in Ilam, Iran. Data on infertility history, obstetric variables (gestational age, preterm birth history, placental disorders, and cervical abnormalities) and fetal outcomes were collected via a 37-item questionnaire. Analyses using SPSS v21 compared PTB recurrence rates and gestational age thresholds (< 34 weeks) between women with and without infertility history, employing chi-square and t-tests (P<0.05 significance).

Results: Among 350 PTB cases, 61 (17.4%) had recurrent PTB. Women with infertility history constituted 23% (14/61) of recurrent PTB cases vs. 3.1% (9/289) in non-recurrent PTB (P=0.001). Critically, all women with infertility history in the recurrent PTB group delivered before 34 weeks (P=0.001), compared to 36.7% (106/289) in non-recurrent PTB. This aligns with studies showing infertility treatments and recurrent pregnancy loss elevate PTB risk.

Conclusion: Infertility history is strongly associated with early recurrent PTB (< 34 weeks), independent of other obstetric factors. These findings underscore the need for targeted prenatal monitoring in women with infertility history, as their risk of early PTB recurrence is 7-fold higher than those without such history.

Keywords: Recurrent Preterm Birth, Infertility History, Early Preterm Delivery

Pnm-26: Examination of Genetic Factors on Infertility: A Review of Current Evidence

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Background: Infertility affects approximately 10–15% of couples globally, with genetic factors contributing significantly to both male and female reproductive dysfunction. Genetic abnormalities including chromosomal defects, gene mutations, and polymorphisms are increasingly recognized as crucial elements in infertility. A better understanding of these factors is essential for enhancing diagnostic accuracy, genetic counseling, and therapeutic strategies.

Materials and Methods: A comprehensive literature review

was conducted through databases such as PubMed, Scopus, and Web of Science. Keywords including “genetic factors,” “infertility,” “chromosomal abnormalities,” and “gene mutations” were used to identify peer-reviewed articles published between 2015 and 2024. Selected studies were analyzed for their findings on the relationship between genetic variations and infertility.

Results: Chromosomal anomalies such as Klinefelter syndrome and Turner syndrome are leading causes of male and female infertility, respectively. Specific gene mutations such as Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) in cases of congenital bilateral absence of the vas deferens and NR5A1 in ovarian insufficiency are also implicated. Additionally, polymorphisms affecting hormonal pathways and DNA repair mechanisms have been linked to reduced fertility. Recent developments in genetic testing, especially next-generation sequencing, have greatly improved the identification and clinical management of these conditions.

Conclusion: Genetic factors play a pivotal role in infertility and must be considered in diagnostic and therapeutic protocols. Early genetic screening can inform personalized treatments and counseling, ultimately improving outcomes in assisted reproductive technologies. Integrating molecular diagnostics into infertility care holds promise for more targeted and effective interventions.

Keywords: Genetic Factors, Infertility, Chromosomal Abnormalities, Gene Mutations, Assisted Reproductive Technology

Pnm-27: Prevention Strategies for Infertility: A systematic review of studies

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Background: Infertility affects 10–15% of reproductive-age couples worldwide and is caused by multifactorial factors including lifestyle, environmental exposures, and genetic predispositions. Recent evidence emphasizes the critical role of preventive strategies focusing on modifiable risk factors to reduce infertility prevalence. This narrative review aims to synthesize recent evidence (2020-2025) on effective infertility prevention strategies with an emphasis on modifiable factors.

Materials and Methods: A comprehensive search was conducted in PubMed, Scopus, Web of Science, and Google Scholar for articles published within the past five years. After excluding review articles, duplicates, irrelevant studies, and books, studies were selected for analysis.

Results: Findings show that adherence to diets rich in antioxidants, fiber, and omega-3 fatty acids -primarily from fruits, vegetables, legumes, and fish- is associated with improved fertility outcomes. Conversely, high intake of red and processed meats correlates with reduced semen quality and ovulatory dysfunction. Adequate vitamin D levels are beneficial for women with polycystic ovary syndrome. Multifaceted interventions like Life's Crucial 9 (LC9), which include physical activity, stress management, and nutritional optimization, potential in lowering infertility risk. However, psychological stress, limited awareness, and healthcare access disparities remain significant

barriers.

Conclusion: Modifiable lifestyle factors play a vital role in infertility prevention. Public health policies should prioritize educational programs promoting balanced nutrition, regular exercise, and mental health support to improve reproductive outcomes. Addressing structural barriers is essential to ensure equitable access to preventive reproductive care.

Keywords: Infertility Prevention, Vitamin D, Nutritional Interventions, Reproductive Health

Pnm-38: Application of Artificial Intelligence in Infertility: Systematic Review of Recent Advances

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Background: Infertility affects 10–15% of couples globally, causing emotional and financial burdens. Advances in artificial intelligence (AI) provide tools to improve diagnosis, treatment, and outcome prediction in reproductive medicine. This review summarizes studies on AI use in infertility management, focusing on assisted reproductive technologies, imaging, and predictive modeling.

Materials and Methods: A comprehensive search was conducted in PubMed, Scopus, and Web of Science for articles published between 2020 and 2025. Using relevant keywords and after excluding review articles, abstracts, duplicates, and books, eligible studies examining AI in diagnosis, treatment, and outcome prediction were selected.

Results: Among 37 eligible studies, AI methods -primarily Machine Learning (ML) and Deep Learning (DL)- were applied in key infertility domains. Comparative analysis showed AI-based embryo selection increased implantation rates by up to 15% compared to conventional grading. Several studies reported accuracy above 85% for AI-assisted sperm analysis and ovarian reserve prediction. However, models varied in input variables, architecture, and validation. We propose a classification framework based on AI application (diagnostic, therapeutic, predictive) and model transparency to aid clinical comparison.

Conclusion: This review proposes a framework to evaluate and classify AI tools in reproductive medicine, supporting clinical decisions and research design. Adoption of AI requires standardized validation, ethical oversight, and collaboration. Integrating AI with local infertility protocols, especially in resource-limited settings like Iran, could enhance accessibility, reduce cost, and improve outcomes.

Keywords: Artificial Intelligence, Infertility, Machine Learning, Assisted Reproductive Technologies

Pnm-29: Innovative Roles of Artificial Intelligence in Infertility Care: A Nursing and Midwifery Perspective

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Background: Infertility is a growing global health concern affecting millions of couples, often leading to emotional and social distress. Artificial Intelligence (AI) is increasingly being integrated into healthcare, offering novel solutions for improving infertility care, especially through nursing and midwifery services.

Materials and Methods: This narrative review included studies published from 2015 to 2024, sourced from PubMed, Scopus, and Web of Science. Selected literature focused on the use of AI in nursing and midwifery aspects of infertility care, including clinical decision support, remote monitoring, individualized treatment planning, and predictive analytics.

Results: AI technologies have improved the accuracy and efficiency of infertility management. Machine learning algorithms are used to predict assisted reproductive technologies outcomes based on patient data. In nursing and midwifery, AI enables the development of personalized care plans and supports remote tracking of patients during treatment. Furthermore, AI-driven tools such as chatbots enhance patient communication and reduce anxiety by providing real-time guidance and emotional support.

Conclusion: The integration of AI into infertility care marks a transformative advancement in nursing and midwifery practice. It offers promising improvements in treatment precision, patient engagement, and overall care quality. However, further research is necessary to validate these technologies and ensure ethical, equitable implementation in clinical settings.

Keywords: Artificial Intelligence, Infertility, Nursing, Midwifery, Assisted Reproductive Technologies, Patient Care

Pnm-30: Environmental Air Pollution and their Effects on Men and Women Infertility: A Comprehensive Review

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Background: Air pollution has emerged as a significant global environmental concern, with widespread consequences for human health. Recent studies indicate that prolonged exposure to air pollutants, including particulate matter, nitrogen dioxide, and carbon monoxide, could potentially compromise reproductive health, leading to infertility in both men and women. This review aims to examine the mechanisms by which air pollution may impair fertility in both genders.

Materials and Methods: This review synthesizes research published from 2015 to 2024, with a focus on the effects of air pollution on reproductive health. Data were extracted from reputable sources such as PubMed, Scopus, and Web of Science. The review analyzes research examining the effects of pollutants on sperm health, ovulation, hormonal regulation, and fetal development. It also addresses the influence of lifestyle choices and socioeconomic factors in moderating these effects.

Results: The analysis of existing studies reveals that exposure to elevated levels of air pollution is correlated with a reduction in sperm count, motility, and quality in men. In women, pollutants have been linked to irregular menstrual cycles, hormonal disruptions, and a reduction in ovarian reserve. Prenatal exposure to pollutants also appears to negatively affect fetal development, increasing the risk of complications during pregnancy. Furthermore, air pollution may contribute to conditions such as

polycystic ovary syndrome, which could further hinder fertility.

Conclusion: Air pollution is increasingly recognized as a critical environmental factor impacting fertility in both men and women. The evidence highlights the urgency of implementing public health policies aimed at reducing exposure to harmful pollutants, particularly in urban settings. Continued research is essential to uncover the biological mechanisms behind these effects and to develop effective preventive strategies.

Keywords: Air Pollution, Infertility, Reproductive Health, Male Infertility, Female Infertility

Pnm-31: The Role of Artificial Intelligence and Digital Innovation in Infertility Care: A Narrative Overview

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Background: Infertility affects 10–15% of reproductive-age couples worldwide and continues to pose a significant public health issue. The emergence of artificial intelligence (AI) and digital technologies in reproductive healthcare has introduced novel possibilities for enhancing diagnostic accuracy, personalizing treatment plans, and enriching patient interactions.

Materials and Methods: This narrative overview compiles insights from scholarly articles published between 2018 and 2024, sourced from databases such as PubMed, Scopus, and Web of Science. The review emphasizes the utilization of AI in areas such as sperm analysis, embryo evaluation, ovarian reserve estimation, and prediction of treatment success. It also explores the contribution of digital health solutions -including mobile apps, wearable sensors, and telehealth services- to infertility care.

Results: AI-driven systems have shown promising precision in analyzing sperm morphology, assessing embryo quality, and predicting ovarian response. Meanwhile, digital technologies support remote monitoring, encourage compliance with treatment plans, and enhance communication between healthcare providers and patients. Together, AI and digital tools are enabling a more tailored and data-informed approach to reproductive treatment.

Conclusion: The integration of AI and digital health solutions marks a transformative shift in how infertility is managed. While existing research highlights their potential to improve both clinical outcomes and patient involvement, further in-depth studies and ethical frameworks are essential to guide their responsible and widespread adoption.

Keywords: AI in Reproductive Health, Infertility Technology, Digital Medicine, Personalized Fertility Care

Pnm-32: The Role of Artificial Intelligence in the Diagnosis and Management of Infertility: A Comprehensive Review of Recent Advances in Male and Female Reproductive Technologies

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Background: Infertility represents a significant global health issue, affecting approximately one in six couples, with male and female etiologies contributing nearly equally. Conventional diagnostic and therapeutic modalities in reproductive medicine are limited by subjectivity, cost, and variable efficacy. Artificial intelligence (AI) has recently emerged as a promising approach to address these limitations.

Materials and Methods: This review synthesizes current advancements in AI applications for the diagnosis and management of infertility, with a comprehensive focus on both male and female reproductive technologies. A narrative review of recent peer-reviewed studies was conducted, encompassing literature published between 2019 and 2025. Inclusion criteria focused on original research involving AI methodologies -such as machine learning, deep learning, and multimodal data integration- applied to infertility diagnostics, treatment optimization, or prognostic modeling within assisted reproductive technologies.

Results: In male infertility, AI has enhanced the precision of semen analysis, facilitated predictive modeling for sperm retrieval in azoospermic patients, and supported clinical decision-making in idiopathic cases. In female infertility, AI has contributed to improved endometrial pathology detection, follicular monitoring, oocyte quality assessment, and embryo selection. Integration of imaging, clinical, and molecular data using AI frameworks has demonstrated improved predictive accuracy for clinical outcomes, including pregnancy and live birth. Explainable AI and federated learning approaches are advancing interpretability and data privacy, respectively.

Conclusion: AI has demonstrated substantial potential to augment diagnostic accuracy and therapeutic outcomes in infertility management. Continued development, validation, and integration of AI systems within clinical workflows are essential to fully realize their utility and ensure ethical, reproducible, and generalizable applications.

Keywords: Artificial Intelligence, Infertility, Assisted Reproductive Technologies, Semen Analysis, Embryo Selection

Pnm-33: The Role and Interventions of Midwifery in the Management of Infertility

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Background: Infertility is a multifactorial health condition that affects approximately 10–15% of couples globally. While biomedical interventions dominate infertility management, the psychological, emotional, and social implications are substantial, particularly for women. Midwives, as integral members of reproductive healthcare teams, have a growing role in the holistic support of individuals experiencing infertility.

Materials and Methods: This review aims to synthesize current evidence on the roles and interventions of midwives in the context of infertility, including psychosocial counseling, educational support, and their involvement in fertility-related decision-making and care. A narrative review methodology was adopted. Relevant peer-reviewed literature published between 2015 and 2025 was reviewed, focusing on midwifery-led interventions for infertile individuals. Sources included clinical trials, qualitative studies, and descriptive surveys. The databases

searched included PubMed, Scopus, and ScienceDirect.

Results: Midwifery interventions address multiple dimensions of infertility care. These include group and individual counseling to reduce perceived stress, support for coping with infertility stigma, enhancement of emotional intelligence, and improving quality of life. Midwives contribute to fertility education, awareness-raising, and correcting misconceptions -especially in underserved or rural populations. Additionally, midwives play a role in adoption counseling, post-assisted reproductive technologies pregnancy care, and transitional support from infertility to parenthood. However, gaps remain in training, awareness of reproductive complications such as genital schistosomiasis, and the standardization of midwifery roles in infertility settings.

Conclusion: Midwives can serve as essential providers of psychosocial and educational support in infertility care. Incorporating structured midwifery-led programs within fertility services may enhance treatment outcomes and psychological well-being. Further research is needed to standardize practices and evaluate the long-term impact of midwifery interventions in infertility management.

Keywords: Midwifery, Infertility, Psychosocial Support, Counseling, Reproductive Health

Pnm-34: The Impact of Complementary and Alternative Medicine (CAM) on Infertility: A Systematic Review

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Background: Infertility is a global public health issue, affecting 3.5-22% of couples worldwide (10.6% in Iran). Despite limited data, growing evidence shows increased use of complementary and alternative medicine (CAM) as either supplements or replacements for conventional infertility treatments. The objective of this study is to examine the role of CAM practitioners in supporting and treating infertility.

Materials and Methods: A review was performed based on the PICO criteria and based on the PRISMA checklist and using PubMed, Web of Science, Google Scholar search engine, and Boolean operators. The time limit between 2010 and 2025 was determined using the MESH keywords “Infertility”, “Complementary and alternative medicine” and “Treatment”. After checking the entry and exit criteria and critically evaluating the quality of the selected articles, 10 articles were included in the study.

Results: A significant percentage of infertile women (65.3%) use CAM methods, especially among those with longer marriage durations and prolonged attempts to conceive. The most common methods include herbal products and religious practices, with family and friends often guiding their use. Additionally, many women believed these methods to be effective, although the actual efficacy requires further research.

Conclusion: Based on findings, the utilization of CAM for infertility treatment is notably prevalent, particularly among young, educated women with lower income levels, among whom herbal products constitute the most commonly used modality. A comprehensive, multidimensional evaluation of infertile women is essential, incorporating detailed inquiry into any CAM practices employed. Healthcare professionals must systematically assess CAM usage among infertile women and

provide them with evidence-based information about these methods.

Keywords: Infertility, Complementary and Alternative Medicine, Treatment

Pnm-35: Investigating The Complications of Intentional Abortion, A Systematic Review

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Background: Abortion is one of the serious and important issues in today's societies, if it occurs in unsafe conditions, the mother's life is in danger. Intentional abortion is an important issue to consider, even though in some societies, abortion is legally performed at the mother's request, but its complications It has been said in few places that the complications of intentional abortion have been investigated in this study.

Materials and Methods: By searching the PubMed and Google Scholar sites and reading more than 30 full-text articles from 2020 to 2024 that are similar to our study on the complications of intentional abortion. This systematic review study will be conducted with the aim of investigating the complications of abortion. They have the criteria for entering the study.

Results: Among 30 articles related to induced abortion, women who reported a previous induced abortion were more likely to deliver preterm before 37 weeks and 34 weeks, with a hazard ratio of 1.18 (95% confidence interval [CI] 1.02–1.36) and 1.65 (95% CI: 1.23–2.21), respectively. The risk of GDM was higher in women who experienced abortion than those who did not (odds ratio [OR] = 1.41 95% CI: 1.28–1.55, $I^2 = 66.8\%$). The risk of GDM increased with increasing number of miscarriages (1 time: OR = 1.67, 95% CI = 1.26–2.22; 2 times: OR = 2.10, 95% CI = 1.26–3.49; ≥ 3 times: OR = 2.49, 95% CI = 1.24–5.01). Both spontaneous abortion (OR = 1.52, 95% CI = 1.30–1.78) and induced abortion (OR = 1.07, 95% CI = 1.03–1.11) were associated with an increased risk of GDM. Having a history of medical abortions, more than 3 surgical abortions, or both medical and surgical abortions was associated with an increased risk of breast cancer in postmenopausal women (OR 2.48; 95% CI, 1.14–5.40). Premenopausal women who used an intrauterine device for more than 20 years had a lower risk of breast cancer than other postmenopausal women at a younger age (OR 0.41; 95% CI 0.25–0.68).

Conclusion: In women who had an intentional abortion, the risk of depression and anxiety, breast cancer, adenomyosis, and chronic diabetes increases. Also, in a study, acute uterine inversion increases in intentional abortions over 14 weeks.

Keywords: Intentional Abortion, Reproductive Health, Quality of Sexual Life, Anxiety, Depression

Pnm-36: The Effect of Aloe Vera Plant on Cytokine Proinflammatory Factor in Polycystic Ovary Syndrome

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Background: Polycystic ovary syndrome is one of the most

common endocrine disorders among women. Inflammatory markers play an important role in managing ovarian function. According to new studies, aloe vera plant has been considered as a medicinal plant due to its anti-inflammatory properties, and some researches have shown that its consumption may be useful for reducing the symptoms of polycystic ovary syndrome (PCOS). Studies on the effects of aloe vera have shown that this herb may improve hormonal symptoms, regulate blood sugar, improve ovarian function, and reduce inflammation associated with PCOS.

Materials and Methods: A literature search was conducted through PubMed and Science direct to identify the effect of Aloe vera on PCOS.

Results: Inflammatory factors such as serum CRP, hs-CRP, IL-1Ra, interleukin 6 (IL-6), IL-17A, IL-17F, IL-18, IL-23, factor decrease necrosis alpha (TNF α), acid glycoprotein α -1, monocyte chemoattractant protein- 1 (MCP-1) and adipokines and their paralogs, including chemerin, C1q and TNF-related 6 (C1QTNF6) were also significantly increased in the peripheral blood of PCOS patients, which according to the studies conducted, aloe vera can reduce inflammatory factors including TNF α , interleukin 6 and IL-1 β ($P < 0.01$ and $P < 0.05$, respectively).

Conclusion: According to the studies conducted in polycystic ovary syndrome, inflammatory factors such as cytokines are also increased, and by giving the active substance of aloe vera plant (hydroalcohol 70%) to people with polycystic ovary syndrome, the level of inflammatory factors can be reduced. and relieved the symptoms.

Keywords: Polycystic Ovary Syndrome, Infertility, Aloe Vera

Pnm-37: Exosomes as A Novel Therapeutic Option for Female Infertility: The Systematic Review

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Background: Infertility is a widespread issue that affects approximately 10-15% of couples globally. Female infertility accounts for half of all infertility cases. Although there have been significant advancements in fertility treatments, for example, assisted reproductive technologies are used to treat female infertility. However, these methods are often invasive, expensive, and carry a risk of multiple pregnancies. Therefore, it is crucial to identify new and effective therapies to address this issue. The application of exosomes has gained attention as a potential therapeutic option for female infertility. This systematic review examines current research on using exosomes for treating female infertility.

Materials and Methods: A comprehensive literature search was undertaken utilizing the PubMed, Scopus, and Web of Science databases while employing the keywords "exosomes," "treatment," and "female infertility." After meticulously screening through twenty-five articles, a thorough review was conducted.

Results: Exosomes are extracellular vesicles derived from stem cells that contain bioactive molecules, such as proteins, lipids,

and various types of RNAs, which makes them valuable in therapeutic applications. Unlike stem cell transplantation, exosome therapy is a cell-free approach that avoids potential risks and limitations, such as immune reactions and losing original cell characteristics. Research has been conducted to study the application of exosomes in various reproductive disorders, and stem cell-derived exosomes have shown great promise as a therapeutic approach for treating female infertility. Based on studies, exosomes derived from mesenchymal stem cells can regulate immune responses, have anti-inflammatory effects, and potentially enhance ovarian function in conditions like polycystic ovary syndrome and premature ovarian failure (POF). Exosomes derived from human amniotic fluid and placenta also improved follicle development and ovulation rates in POF patients. In general, exosomes derived from ovarian cells promote the proliferation and survival of oocytes. Research shows exosomes contribute to endometrial receptivity in recurrent implantation failure and improve implantation rates. Studies showed that exosomes as indicative biomarkers in endometriosis have significant potential to improve this disease.

Conclusion: Although exosome-based therapies show promise in treating female infertility, more research is needed to fully understand their mechanisms of action and establish their safety and efficacy in clinical settings. Ongoing studies are aimed at optimizing treatment strategies and overcoming the challenges associated with exosome therapy for female infertility.

Keywords: Exosomes, Therapeutic Option, Female Infertility

Pnm-38: Digital Health Technologies and Their Role in Improving Infertility Treatments

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Background: Infertility is a global health challenge affecting millions of individuals and couples worldwide. With advancements in digital health technologies, there is growing potential to revolutionize infertility treatments. This systematic review aims to evaluate the role of digital health technologies, including mobile applications, wearable devices, telemedicine, and artificial intelligence (AI), in improving the diagnosis, management, and treatment outcomes of infertility.

Materials and Methods: The present study was conducted as a systematic review. After studying and evaluating 50 original and systematic review articles in databases such as PubMed, Scopus, and Semantic Scholar by searching using the keywords "Digital Health Technologies", "Infertility Treatments", "Fertility Improvement", "Assisted Reproductive Technology", "Artificial Intelligence" from 2019 to February 2025, 15 articles were selected and reviewed.

Results: The findings indicate Digital health technologies are revolutionizing infertility care by integrating innovative tools and approaches. These advancements are enhancing patient engagement, treatment precision, and accessibility. Mobile apps empowered patients to track menstrual cycles, ovulation, and lifestyle factors, while providing healthcare providers with data for personalized care. Wearables monitored physiological parameters like basal body temperature and sleep, enhancing treat-

ment precision. Telemedicine improved access to care, especially in remote areas, through virtual consultations and support groups. AI improved diagnostic accuracy, predicted treatment success, and optimized ART protocols. Together, these technologies increased patient satisfaction, treatment adherence, and clinical outcomes, advancing infertility care significantly.

Conclusion: Digital health technologies have the potential to transform infertility care by enhancing accessibility, personalization, and efficiency. However, challenges such as data privacy, regulatory issues, and the need for further clinical validation remain. Future research should focus on integrating these technologies into standard care protocols and evaluating their long-term impact on infertility treatment outcomes.

Keywords: Digital Health Technologies, Infertility Treatments, Fertility Improvement, Assisted Reproductive Technology, Artificial Intelligence

Pnm-39: Artificial Intelligence and Ethics in Infertility Treatment: Challenges and Opportunities

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Background: Artificial intelligence (AI) is increasingly being integrated into infertility treatments, offering innovative solutions for diagnosis, treatment optimization, and patient care. However, the rapid adoption of AI in this sensitive field raises significant ethical concerns. This systematic review explores the challenges and opportunities associated with the use of AI in infertility treatment, focusing on ethical considerations, patient outcomes, and the potential for improving reproductive healthcare.

Materials and Methods: The present study was conducted as a systematic review. After studying and evaluating 30 original and systematic review articles in databases such as PubMed, Scopus, and Semantic Scholar by searching using the keywords "artificial intelligence", "infertility", "ethics", "infertility treatment", "challenges and opportunities" from 2020 to February 2025, 12 articles were selected and reviewed.

Results: The integration of AI into infertility treatments has shown promising results in improving diagnostic accuracy and treatment personalization. Studies highlight that AI can analyze vast amounts of data, such as medical imaging and genetic information, to provide insights that enhance decision-making. However, ethical concerns remain a significant barrier. Issues like data privacy, algorithmic bias, and the potential for misdiagnosis due to flawed algorithms need to be addressed. Additionally, the lack of transparency in how AI systems operate can hinder patient trust. Despite these challenges, the potential benefits of AI, such as reducing treatment costs and increasing accessibility, make it a valuable tool in advancing reproductive healthcare.

Conclusion: While AI holds great promise for advancing infertility treatment, its ethical implications cannot be overlooked. Addressing challenges such as data privacy, algorithmic bias, and transparency is critical to ensuring that AI is used responsibly and equitably in reproductive healthcare. Future research should focus on developing ethical frameworks and guidelines

for AI applications in infertility treatment, as well as evaluating the long-term impact of AI on patient outcomes and healthcare systems.

Keywords: Artificial Intelligence, Infertility, Ethics, Infertility Treatment, Challenges and Opportunities

Pnm-40: The Role of Calcium and Manganese in Improving Sperm Quality: A Systematic Review

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Background: Calcium and manganese, as essential minerals, play a crucial role in physiological processes related to reproduction. Given the prevalence of male fertility issues and their association with deficiencies in these elements, investigating the effects of calcium and manganese supplementation on sperm quality can enhance our understanding of fertility-related factors and contribute to the development of new therapeutic protocols. This systematic review analyzes the existing evidence on the relationship between these elements and sperm quality.

Materials and Methods: This systematic review was conducted in February 2025 in five stages: formulating the research question, searching databases, extracting and selecting relevant studies, tabulating information, and analyzing the data. The literature search was performed in PubMed, Magiran, IranDoc, ScienceDirect, and Google Scholar using relevant keywords. The initial search yielded 285 articles, which were screened based on inclusion and exclusion criteria using the PRISMA 2020 flowchart, resulting in the selection of 21 observational studies published between 2011 and 2024 for final analysis.

Results: Of the 21 included studies, 11 examined the effects of calcium, and 10 focused on manganese in relation to sperm quality. The findings indicated that adequate calcium levels are associated with increased sperm motility, while calcium deficiency leads to reduced motility and fertilization capacity. Calcium also plays a key role in sperm capacitation and oxidative stress reduction. Similarly, studies on manganese demonstrated its positive effects on sperm motility, viability, and metabolism, as well as its function as a potent antioxidant.

Conclusion: This systematic review suggests that calcium and manganese supplementation positively influence sperm quality, particularly by enhancing motility and fertilization potential. These effects are likely mediated through biochemical mechanisms related to energy metabolism and antioxidant properties. The findings of this study may contribute to the development of new strategies for improving male fertility and highlight the importance of essential nutrients in reproductive health.

Keywords: Calcium, Manganese, Sperm Quality, Male Fertility

Pnm-41: Overview of The Relationship between Vaginal Microbiome Changes and IVF Success and Pregnancy Outcomes

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Background: Changes in the vaginal microbiome significantly influence women's fertility and the outcomes of assisted reproductive technologies like *in vitro* fertilization (IVF). An imbalanced microbiome can lead to inflammation and dysbiosis, negatively affecting reproductive health. This review examines the relationship between vaginal microbiome alterations and their effects on IVF success and pregnancy outcomes.

Materials and Methods: This systematic review was conducted in February 2025 and involved five stages: formulating the research question, executing a comprehensive literature search, extracting relevant studies, selecting articles, and reporting results. Searches were performed using keywords in databases such as PubMed, Scopus, Google Scholar, Science Direct, and Iran Doc. The initial search identified 687 articles. After applying inclusion and exclusion criteria as per the PRISMA 2020 flow diagram, 13 observational studies published between 2021 and 2025 were included. Quality of the studies was evaluated using the Kessels quality assessment tool, yielding scores of 9 (1 study), 8 (5 studies), 7 (6 studies). Data were organized based on biological factors, microbiome disorders, and psychological-social influences.

Results: This review identified several key complications linked to changes in the vaginal microbiome, categorized into three areas: 1. Biological Factors: - Inflammation and Tissue Damage: Dysbiosis can cause inflammation in reproductive tissues, impairing fertility and increasing risks. Chronic inflammation may lead to anatomical changes that hinder conception. - Altered Gamete Quality: Changes in the microbiome negatively impact egg and sperm quality, contributing to higher infertility rates. 2. Microbiome Disorders: - Non-Lactobacillus Dominance: The presence of non-Lactobacillus species in the vaginal microbiome is associated with decreased live birth rates following IVF/ICSI. 3. Psychological and Social Factors: - Mental Health Impact and Psychological Stress: Chronic infections can negatively affect mental health and increase stress levels, complicating the journey to conception.

Conclusion: These findings emphasize the importance of evaluating the relationship between vaginal microbiome changes and IVF success. Optimizing the vaginal microbiome may represent a novel strategy to enhance fertility treatment results.

Keywords: Vaginal Microbiome, IVF Success, Pregnancy Outcomes, Infertility

Pnm-42: Polycystic Ovary Syndrome with Metabolic Syndrome and Diabetes: A Systematic Review and Meta-Analysis

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Background: Polycystic ovary syndrome (PCOS) is linked to metabolic syndrome (MetS) and diabetes mellitus (DM), highlighting the need to understand these associations for better clinical management and prevention.

Materials and Methods: A systematic search was done in PubMed, Scopus, Web of Science, Embase, and Cochrane CENTRAL for studies published between 1990 and 2025, following PRISMA guidelines. We included observational studies evaluating the link between PCOS and DM or MetS. Data were collected using a standard checklist, and study quality was evaluated with the Newcastle-Ottawa Scale. Pooled relative risks (RR) were estimated using a random-effects model, and heterogeneity was assessed with the Cochrane Q and I^2 tests. Subgroup analyses considered diagnostic criteria, study design, geography, publication year, DM type, age, and body mass index.

Results: Of 3,747 articles, 44 studies on DM and six studies on MetS were included. PCOS women had a 72% higher risk of developing DM (pooled RR: 1.72, 95% confidence interval [CI]: 1.43–2.06, $I^2=99.35\%$) than those without PCOS, particularly under Rotterdam criteria (RR: 1.86, 95% CI: 1.79–1.93). The risk was highest for gestational DM (RR: 2.05, 95% CI: 0.89–4.75) and in women aged > 40 years (RR: 1.88, 95% CI: 1.11–3.16). For MetS, PCOS raised the risk by 48% (RR: 1.48, 95% CI: 1.15–1.90, $I^2=74.78\%$), particularly when diagnosed using NIH criteria (RR: 3.41, 95% CI: 1.86–6.26). Geographic variations showed higher DM rates in Europe (RR: 1.97, 95% CI: 1.90–2.05) and MetS in Asia (RR: 1.99, 95% CI: 1.44–2.75). Heterogeneity was high across the analyses, influenced by the diagnostic criteria, study design, and regional differences. No significant publication bias was detected.

Conclusion: PCOS significantly increases the risk of DM and MetS. Standardized diagnostics and longitudinal studies improve risk assessment and personalized management of PCOS metabolic complications.

Keywords: Polycystic Ovary Syndrome, Metabolic Syndrome, Diabetes Mellitus, Meta-Analysis

Pnm-43: Advancements of Mobile Applications in Infertility Interventions: A Review of Current Trends and Evidence

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Background: Numerous mobile applications that help with ed-

ucation, diagnosis and lifestyle changes have been designed in response to the increasing incidence of infertility. Whilst these apps are becoming more and more popular, less is known about their quality, utility and therapeutic effects. This review evaluates mobile applications designed for infertility management.

Materials and Methods: With the help of relevant research databases (Web of Science, MEDLINE, PubMed, Cochrane, CINAHL) and app stores (Apple App Store, Google Play Store), a systematic search was conducted for apps and studies published in English from January 2004 to December 2024. The keywords "telemedicine," "mobile applications," and "infertility" were used. Studies and applications that addressed lifestyle modifications, education, diagnostic support, or infertility treatment that had measurable outcomes were included. Exclusion criteria were studies that did not specifically mention infertility treatment or that just discussed basic menstrual health.

Results: Twenty-one of 76 studies and apps met the inclusion criteria and were categorized into five types: educational, diagnostic, monitoring, lifestyle management, and specialized infertility support apps. Qualitative studies suggest that educational apps and peer-support features improve decision-making, mental health, and user engagement. Ovulation tracking apps outperformed traditional methods in terms of accuracy, increasing pregnancy rates. Studies on at-home sperm analysis apps are relatively new, requiring further research. The effect of apps on medication adherence and appointment attendance is not well documented. Although lifestyle management applications promote healthy habits, few of them address issues specific to infertility. The app's quality was average at best due to issues with usability and content reliability.

Conclusion: There is potential for managing infertility using mobile applications, particularly in the areas of ovulation tracking, education, and emotional support. Further research is needed for assessing the effectiveness of sperm analysis apps and treatment adherence. Medical guidance tailored to each patient can maximize their benefits.

Keywords: Infertility, Mobile Applications, Telemedicine

Pnm-44: The Relationship of Education level with childbearing in women with Systemic Lupus Erythematosus

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Background: Systemic lupus erythematosus (SLE) is a concern for women's childbearing. Education level maybe decreases their concern and help to tolerate and relieve SLE. This study aimed to assess the relation of education level with women's childbearing.

Materials and Methods: This study was conducted on 429 women of reproductive age (15–49 years) with SLE. Research was conducted from January 21, 2023, to March 20, 2024 in the rheumatology clinic and Iranian Lupus Association of Tehran, Iran. Data was randomly collected through an online questionnaire. The data collected instruments included researcher making questionnaires (childbearing variables: the category of pregnancies, birth, and children numbers (0, 1-2, 3-4, more than 4) before and after contracting SLE; Contraceptives (hormo-

nal, IUD, condom, none)). The collected data were entered into SPSS software version 27 and analyzed using Kendall's Tau test at a significant level of $P < 0.01$.

Results: There was a significant relationship between the education level of women, the number of pregnancies ($R: -0.373$, $P < 0.001$, confidence interval [CI] 95%: -0.44 to -0.29), the number of birth ($R: -0.327$, p value < 0.001 , CI 95%: -0.40 to -0.25) and the number of children ($R: -0.377$, $P < 0.001$, CI 95%: -0.44 to -0.30) before contracting SLE. Also, study showed significant relationship between the education level of women and contraceptive use ($R: -0.145$, $P: 0.003$, CI 95%: -0.24 to -0.04).

Conclusion: Education level just has relation with childbearing characters before contracting SLE and it lonely has not relation with childbearing characters after contracting SLE. But Women with higher levels of education had lower rates of using hormonal contraceptive.

Keywords: Education, Systemic Lupus Erythematosus, Women, Childbearing

Pnm-45: How Viral Infections Can Affect Your Fertility

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Background: This overview looks at how common viral infections -like HIV, HPV, and herpes- might impact a person's ability to have children. Understanding these links can help improve prevention and treatment options.

Materials and Methods: We reviewed studies from PubMed, Scopus, and ISI Web of Science using keywords like "viral infections," "infertility," "HIV," "HPV," and "herpes." We included research published up to 2024, such as clinical trials and observational studies. The focus was on how these viruses affect fertility, how they are diagnosed, and what treatments help.

Results: The evidence shows that some viruses can seriously affect fertility. HIV, for example, has been linked to hormonal issues and poorer sperm quality in men. HPV can infect reproductive tissues and cause problems getting pregnant. Herpes viruses, like HSV and Epstein-Barr, can cause inflammation and damage in reproductive organs, making conception more difficult. On the bright side, antiviral medicines can improve fertility outcomes for infected people. However, many people carry these viruses without symptoms, which makes early testing important in infertility assessments.

Conclusion: Viral infections are an important, sometimes overlooked, factor in infertility. Regular screening and early treatment can make a big difference. As research advances, developing vaccines and new antiviral drugs will be key to protecting reproductive health worldwide.

Keywords: Viral Infections, Infertility, HIV, HPV, Herpes

Pnm-46: How Bacterial Infections Affect Fertility

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Background: This overview looks at how bacterial infections can cause infertility in both women and men. Picking common bacteria like *Chlamydia* and *gonorrhea*, it explores how these infections lead to reproductive issues and what can be done to diagnose and treat them effectively.

Materials and Methods: We reviewed scientific articles from PubMed, Scopus, and ISI databases. Using keywords like "bacterial infection," "infertility," "Chlamydia," "pelvic inflammatory disease," and "male infertility," we gathered studies published up to 2024. The focus was on understanding how common these infections are, how they damage reproductive organs, and what treatments are most successful.

Results: The evidence shows that bacterial infections such as *Chlamydia* and *gonorrhea* can seriously harm fertility. In women, these infections often ascend into the fallopian tubes, causing inflammation and scarring that block the egg's path -leading to infertility. In men, these bacteria can affect sperm production and quality. Finding infections early through reliable testing and treating them promptly with antibiotics can help prevent long-term damage. Unfortunately, many people don't know they're infected because they don't show symptoms, which makes regular screening important.

Conclusion: Bacterial infections are a preventable cause of infertility. Increasing awareness, improving diagnostic tools, and providing quick, effective treatment are key steps in helping couples conceive. Ongoing research into antibiotic resistance and vaccines will also help protect future generations from these issues.

Keywords: Bacterial Infections, Infertility, Chlamydia, Pelvic Inflammatory Disease, Male Fertility

Pnm-47: How Sclerotherapy Might Help Treat Infertility Caused by Pelvic Vascular Issues

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Background: This study looks at whether sclerotherapy -a minimally invasive procedure- can be effective in treating ovarian or pelvic blood vessel abnormalities that may contribute to infertility in women.

Materials and Methods: We reviewed articles from PubMed, Scopus, and ISI Web of Science published up to 2024. We searched for terms like "sclerotherapy," "infertility," "ovarian vascular anomalies," and "pelvic malformations." The focus was on case reports and retrospective studies where women with diagnosed blood vessel issues in the pelvis or ovaries underwent sclerotherapy. We analyzed the success rates, pregnancy outcomes, and any complications.

Results: The findings suggest that sclerotherapy can significantly reduce abnormal blood vessels in the pelvis, which are often linked to pelvic congestion syndrome and ovarian problems. Many women reported relief from symptoms and improvements in ovarian function after the procedure. Importantly, fertility outcomes were promising -some women were able to conceive naturally, while others had success with assisted reproductive techniques, usually within a year after treatment. Overall, the procedure was safe, with only minor side effects like temporary pelvic pain.

Conclusion: Sclerotherapy looks like a safe and effective op-

tion for women dealing with pelvic blood vessel problems that affect fertility. It's minimally invasive and may help improve ovarian blood flow and function, increasing the chances of conception. Still, more research with larger groups of women is needed to confirm these benefits and develop clear guidelines.

Keywords: Sclerotherapy, Infertility, Ovarian Blood Vessels, Pelvic Congestion, Minimally Invasive

Pnm-48: Dietary Antioxidant Potential and Male Infertility: Evaluating The Evidence for DTAC

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Background: Male infertility is a multifaceted health issue contributing to nearly half of all infertility cases worldwide. Among the numerous etiological factors, oxidative stress has emerged as a pivotal mechanism impairing sperm quality and function. Dietary total antioxidant capacity (DTAC), representing the cumulative antioxidant potential of the diet, may influence the redox balance in the male reproductive tract and thus affect fertility outcomes. This review aims to critically examine the association between DTAC and male infertility by evaluating current evidence on how dietary antioxidant intake modulates oxidative stress, semen parameters, and reproductive performance in men.

Materials and Methods: A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science databases for studies published up to 2025, using search terms such as "Dietary Total Antioxidant Capacity," "DTAC," "male infertility," "oxidative stress," and "semen quality." Both observational and interventional studies were reviewed to provide a multidimensional understanding.

Results: The evidence suggests a potential protective role of higher DTAC against oxidative damage in spermatozoa. Several studies have reported positive correlations between high dietary antioxidant intake and improved sperm concentration, motility, morphology, and DNA integrity. However, inconsistencies across studies regarding dietary assessment methods, antioxidant databases, and confounding factors necessitate cautious interpretation of the findings.

Conclusion: DTAC may serve as a promising, non-invasive biomarker for evaluating dietary influences on male reproductive health. Optimizing antioxidant intake through diet could represent a cost-effective and accessible strategy to mitigate oxidative stress-related male infertility. Nonetheless, further longitudinal studies and randomized controlled trials are essential to establish causality and develop evidence-based dietary guidelines in andrology.

Keywords: Dietary Total Antioxidant Capacity, Male Infertility, Oxidative Stress, Semen Quality, Reproductive Health

Pnm-49: Fertility on the Plate: Impact of Specific Diets on ART Outcomes- A Narrative Review

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Background: Infertility is a growing reproductive health challenge, with assisted reproductive technologies (ART) serving as a key treatment. However, ART success rates vary significantly and are influenced by numerous modifiable factors, including diet and nutrition. Specific dietary patterns may impact ART outcomes by improving gamete quality, hormonal regulation, and endometrial receptivity. This study examines the association between specific dietary patterns such as the Mediterranean diet, antioxidant-rich diets, and low glycemic index diets and ART success rates.

Materials and Methods: This systematic review assessed studies published up to 2025, investigating the association between dietary patterns such as the Mediterranean diet, antioxidant-rich diets, and low glycemic index diets and ART or *in vitro* fertilization (IVF) outcomes. Literature searches were conducted in PubMed, Scopus, Web of Science, and Google Scholar using a combination of MeSH terms ("ART," "IVF," "fertility") and keywords ("nutrition," "dietary patterns"), linked by Boolean operators. Reference management and duplicate removal were performed using EndNote.

Results: The findings indicate that adherence to diets rich in vegetables, fruits, whole grains, legumes, nuts, low-fat dairy, and omega-3 fatty acids is associated with improved ART outcomes. Positive effects include enhanced oocyte and sperm quality, greater endometrial receptivity, lower miscarriage risk, and higher implantation and live birth rates. In contrast, diets high in processed meats, refined sugars, and saturated fats were linked to poorer gamete quality and reduced ART success. Among dietary patterns, the Mediterranean and pro-fertility diets demonstrated the strongest evidence of benefit.

Conclusion: Healthy dietary patterns are associated with better ART outcomes. While more interventional studies are required to confirm causality, the integration of nutrition counseling into fertility care is recommended due to its safety, affordability, and broader health benefits.

Keywords: ART Outcomes, IVF Success, Fertility Diet, Dietary Patterns, Reproductive Nutrition

Pnm-50: Bacterial Vaginosis and Infertility: Examining Mechanisms and Effects

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Background: Bacterial vaginosis (BV) is a common vaginal disorder characterized by an imbalance in the vaginal microbiome, where beneficial lactic acid-producing bacteria decrease while anaerobic bacteria like *Gardnerella vaginalis* increase, leading to disrupted vaginal health; this study specifically investigated the mechanisms through which BV contributes to infertility, focusing on the pathogenic effects of bacterial overgrowth and their impact on reproductive function.

Materials and Methods: This study was a systematic review conducted by searching the PubMed, ProQuest, Scopus, WOS, Cochrane Library, and Google Scholar databases for English-language articles published between 2000 and 2025. The keywords "Bacterial Vaginosis," "Infertility," "Mechanism," "Vaginal microbiome," and "Reproductive Health" were used, combined with the Boolean operators "OR" and "AND." After removing duplicate articles, a final selection of 22 eligible articles were chosen and reviewed.

Results: BV impairs female fertility through multiple mechanisms: it disrupts the vaginal microbiome, increasing pH and reducing sperm survival; produces enzymes that damage sperm structure; triggers inflammation leading to pelvic disease and fallopian tube damage; forms biofilms that perpetuate infection; and increases STI risk 3-4-fold. These effects collectively create an unfavorable reproductive environment, reducing both natural conception and IVF success, emphasizing BV's role as a key modifiable infertility factor requiring prompt treatment.

Conclusion: BV contributes to infertility by disrupting vaginal flora, causing inflammation, and impairing sperm function. Key solutions include: early screening, probiotic treatment (especially *Lactobacillus*), and targeted screening in high-risk areas. Prevention requires sexual health education and addressing risk factors.

Keywords: Bacterial Vaginosis, Infertility, Mechanism, Vaginal Microbiome, Reproductive Health

Pnm-51: The Role of Peer Support in Palliative Care after Abortion and Its Impact on Maternal Mental Health

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Background: Palliative care following abortion is crucial for supporting women's emotional and psychological well-being, particularly in conservative societies where stigma may intensify distress. This study aimed to explore the impact of peer-based palliative care on the mental health of women who have experienced abortion.

Materials and Methods: A peer support group was formed, consisting of women with a history of abortion who met regularly to share personal experiences and emotional challenges. The researcher, serving as the facilitator, guided the sessions based on core palliative care principles such as empathy, active listening, and emotional validation. Data were collected through participant observation and semi-structured interviews and analyzed using thematic analysis.

Results: The findings indicated that peer interactions had a positive effect on participants' mental health. Women reported feeling understood, less isolated, and emotionally relieved through shared dialogue with others who had similar experiences. Key emerging themes included mutual empathy, emotional release, and a sense of belonging. Participants also emphasized that the presence of a trained facilitator contributed to the emotional safety and cohesion of the group.

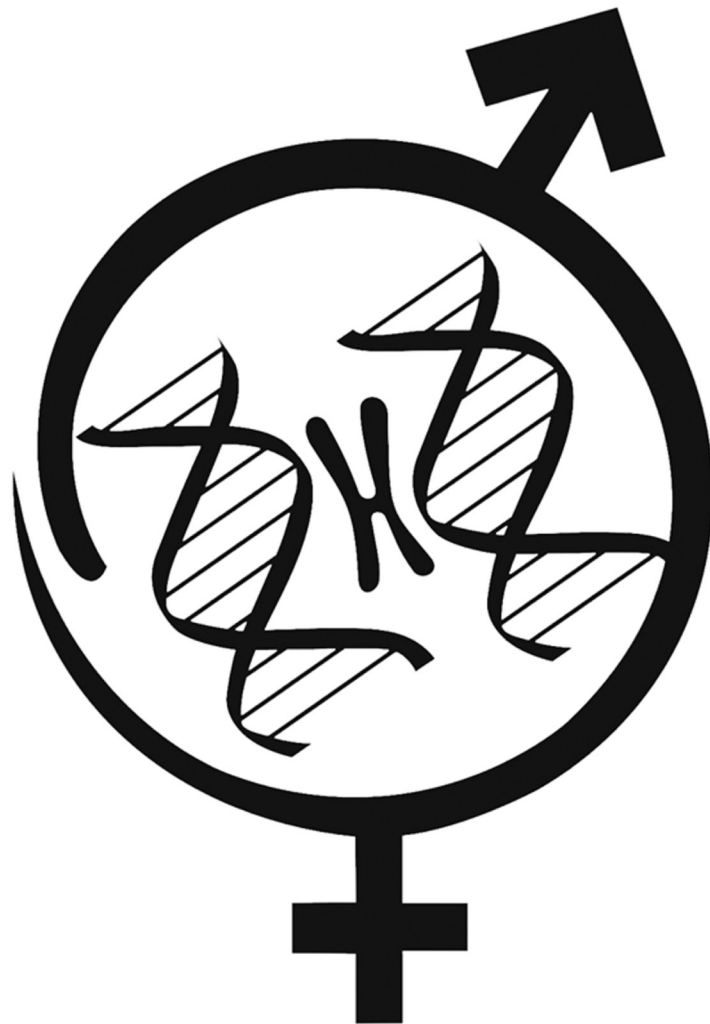
Conclusion: Peer-based palliative care can be an effective approach to enhance the mental health of women following abortion. Structured peer dialogue in a safe and supportive environment may reduce emotional suffering and foster resilience. These findings highlight the need to integrate peer support frameworks into post-abortion care services.

Keywords: Palliative Care, Abortion, Peer Support, Mental Health

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Abstracts of
Royan International Hybrid Twin Congress
21th Congress on Stem Cell Biology and Technology
3-5 September 2025



Royan Institute

Cell Science Research Center

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Abstracts of the 21th Congress on Stem Cell Biology and Technology (2025)

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Sharif Moradi

Dear colleagues,

It is my pleasure to invite you to the **21st Royan International Congress on Stem Cell Biology and Technology, taking place in Tehran, Iran**, from September 3 to 5, 2025. This prestigious event will feature lectures from esteemed global experts, as well as plenary sessions, workshops, and poster presentations, providing a robust platform for scientific exchange.

Following the success of our past events, this congress will continue to lead in disseminating cutting-edge research in stem cells and regenerative medicine. We anticipate bringing together distinguished researchers, scientists, clinicians, trainees, and students to discuss critical advancements in both basic and translational research.

Organized by the Royan Institute for Stem Cell Biology and Technology, this annual conference fosters the exchange of ideas and experiences in stem cell research, developmental biology, bioengineering, and regenerative medicine. We are honored to host this significant event in Tehran, a city rich in natural beauty, history, and culture.

We warmly welcome you to join us in Tehran to share and learn about the latest developments in stem cell research, reconnect with colleagues, and form new collaborations.

I look forward to your participation in 2025 September.

Sincerely,
Sharif Moradi, Ph.D.
Scientific Secretary,
**21st Royan International Congress on
Stem Cell Biology and Technology**

Invited Speakers

Is-1: The Challenges of Pluripotent Stem Cell-Based Germline Chimeras in Rabbits

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Pluripotent stem cells have long been used to produce knockout mice via germline chimera technology. However, aside from the rat, this approach has not been successfully applied to other mammals. I will describe our long-term efforts to generate rabbit embryonic stem cell (ESC) and induced pluripotent stem cell (iPSC) lines. Building on our investigation of the pluripotency continuum in rabbit embryos, I will demonstrate that rabbit iPSCs can be reprogrammed using KLF2, ERAS and PRMT6, which enables them to efficiently colonize host embryos. These chimeric embryos develop into fetuses and newborn rabbits, with iPSCs contributing up to 100 % to certain organs. Notably, female rabbits generated via this method are healthy and transmit the iPSC genome to their offspring, confirming germline chimerism. This advancement lays the groundwork for developing rabbit models of human disease and, when extended to non-human primates, could enable the generation of monkey models that capture complex genetic traits beyond the scope of conventional CRISPR-based embryo editing.

Is-2 Cross-Species Pluripotency Engineering: Mice, Giant Panda, and Guinea Pig

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Pluripotent stem cells are foundational tools for both regenerative medicine and species conservation. Dr. Liu's research portfolio spans multiple breakthroughs across species, each representing a milestone in stem cell innovation. In mice, his group established that SALL4 alone is sufficient to reprogram fibroblasts into iPSCs, offering a minimal-factor strategy for high-efficiency reprogramming and revealing unique synergistic pathways when combined with OCT4. In a major step toward applying stem cell technologies for conservation, his team generated the first iPSCs from the endangered giant panda using a non-integrating episomal vector system. By formulating a panda-specific chemically defined culture medium (FACL) and mapping pluripotency-maintaining signaling pathways, they demonstrated tri-lineage differentiation and opened new avenues for panda gametogenesis and assisted reproduction. In parallel, the team derived epiblast stem cells from post-implantation guinea pig embryos (gpEpiSCs) -marking the first stable pluripotent stem cell lines in this species. These cells exhibit primed-state features, multilineage potential, and both conserved and species-specific regulatory signatures, enhancing the guinea pig's value in disease modeling and cross-species pluripotency comparison. Together, these studies redefine how pluripotency can be captured, stabilized, and applied across diverse mammalian species -from laboratory models to endan-

gered wildlife.

Is-3: Exosome Therapy in Regenerative Medicine: Clinical Application for COVID-19 and Pulmonary Fibrosis Complications

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Human mesenchymal stromal cell-derived small extracellular vesicles (MSC-sEVs), especially those derived from placental sources, are emerging as promising cell-free therapeutic agents due to their regenerative, immunomodulatory, and anti-fibrotic properties. This study evaluated the therapeutic potential of human placental MSC-sEVs (hPMSC-sEVs) in two severe pulmonary conditions characterized by inflammation and fibrosis: systemic sclerosis-associated interstitial lung disease (SSc-ILD) and COVID-19-related acute respiratory distress syndrome (ARDS). In the first clinical trial, ten patients with progressive SSc-ILD received five consecutive daily intravenous doses of hPMSC-sEVs. Clinical parameters including peripheral oxygen saturation (SaO₂), six-minute walk test (6MWT), SF-36 quality of life score, Rodnan skin score, Pittsburgh Sleep Quality Index (PSQI), and pulmonary function tests were assessed at baseline and three months after treatment. Significant improvements were observed in 6MWT (from 187 ± 114.89 to 229 ± 88.24 meters, P = 0.018) and SF-36 score (from 88.30 ± 5.53 to 91.40 ± 6.50, P = 0.015), with non-significant but favorable trends in Rodnan skin score and PSQI. No adverse events were reported. In a separate double-blind, randomized controlled trial on critically ill COVID-19 patients with ARDS, 45 patients received either standard care plus placebo (n=24) or standard care plus hPMSC-sEVs (n=21). The intervention group showed significantly reduced mortality (19.04% vs. 54.16%, P = 0.015) and longer time to death (28.06 vs. 11.10 days, P < 0.001), with balanced baseline characteristics apart from a lower admission SpO₂ in the intervention arm (P = 0.008). Overall, hPMSC-sEVs demonstrated a favorable safety profile and potential clinical benefits in both studies, supporting their further investigation as a novel approach to managing complex pulmonary diseases through immunomodulation and tissue repair.

Is-4: Defining Milestones of Trophectoderm Fate Progression and Naïve-to-Primed Pluripotency Transition in Human Embryos Reveals Stage-Match of Human Blastoids

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Deciphering the molecular events underlying human embryo development during the peri-implantation window is essential to improve medically assisted reproduction. Here, we present a biologically curated transcriptomic atlas of human embryos spanning 3 to 14 days post-fertilization (d.p.f.). Through weighted gene co-expression network analysis, we identified lineage-specific gene modules and revealed progressive ac-

quisition of cell identities. We uncovered that ZIC3 and ZSCAN10 are present during the naïve-to-primed transition in human embryos. We characterized transcriptional regulators of the trophoblast lineage, and inferred the upstream gene regulatory network (GRN) using SCENIC, suggesting putative drivers of polar maturation. Taking advantage of proteomic data, we substantiated the developmental staging of stem cell models, associating human trophoblast stem cells with 8 d.p.f. trophoblast. Lastly, we assessed two extended-culture blastoid models, demonstrating that they recapitulate key molecular features of peri-implantation embryos. Our integrated resource -including scRNA-seq, GRN inference and immunofluorescence- is browsable through an interactive interface at <https://humanembryo-ui.bird.glicid.fr/>.

Is-5: From Stem Cells to Gene Rescue: A New Era of Pluripotency, Precision Reproduction, and the Guinea Pig as ANext-Generation Model for Human Disease

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Despite their physiological proximity to humans, guinea pigs have remained genetically underutilized due to the absence of pluripotent stem cell systems, reproductive tools, and scalable gene therapy platforms. In this study, we present a comprehensive strategy that positions the guinea pig as a powerful next-generation model for human disease. We first establish and characterize guinea pig epiblast stem cells (gpEpiSCs) derived from post-implantation embryos. These cells exhibit hallmark features of primed pluripotency, including expression of OCT4, SOX2, and NANOG, stable karyotypes, and a requirement for FGF2/ACTIVIN A signaling. Maintenance of their pluripotent state further depends on WNT inhibition, and multi-omics analysis reveals both conserved and species-specific transcriptional and epigenetic landscapes. To enable downstream germline transmission, we develop optimized protocols for superovulation and embryo transfer, achieving early success in assisted reproduction. These tools pave the way for future transgenic and gene-editing studies in guinea pigs. Finally, we demonstrate the translational potential of the model through AAV9-mediated Gulo gene therapy in both Gulo-knockout mice and guinea pigs, recapitulating and rescuing the pathological features of Vitamin C deficiency. Treated animals exhibit restored survival, improved neuromuscular function, and metabolic correction, validating this system as a platform for in vivo therapeutic intervention. Together, this integrated pipeline-from stem cell derivation to gene rescue-repositions the guinea pig at the frontier of preclinical research, offering a versatile and human-relevant platform for disease modeling, regenerative biology, and gene therapy innovation.

Is-6: Re-Activation of Progenitor Cellular Program in Cancer Progression and Metastasis

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Cancer stem cells (CSCs) are increasingly recognized as key cells of origin that drive tumour initiation, heterogeneity and therapy resistance. In parallel, pathological dedifferentiation-the regression of mature tumour cells toward a more embryonic-like state- remains a hallmark of aggressive disease across cancer types. Although often studied independently, mounting evidence suggests these phenomena are mechanistically intertwined: plasticity-inducing signals in the tumour microenvironment and epigenetic reprogramming can both generate CSC-like states de novo and sustain pre-existing CSC pools. In this talk I will discuss recent genomic and lineage-tracing data that clarify where, when and how CSCs arise through dedifferentiation cascades. I will further highlight emerging therapeutic strategies that exploit this connection. Understanding and manipulating the CSC-dedifferentiation axis promises more durable responses by eliminating both the seeds and the soil of cancer progression.

Is-7: Looking Ahead: A Roadmap for Multi-Modal Patient Phenotyping

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Advances in artificial intelligence, alongside progress in digital health, biomarker science, imaging, and genomics, are creating new opportunities for more comprehensive and personalized patient phenotyping. This talk outlines a practical framework for integrating these modalities to support early risk detection, clinical decision-making, and research applications. Drawing on real-world experience deploying digital cognitive assessments, analyzing large-scale decentralized trials, and developing biomarker-based tools, I will highlight both the opportunities and challenges presented by AI-driven approaches. Particular emphasis will be placed on implementation realities, data and AI infrastructure needs, and potential collaboration pathways. Attendees will leave with new perspectives to help shape the future direction of their work and the field.

Is-8: Repurposing Drugs for FLT3-Mutated AML: Unlocking New Therapeutic Avenues with Diabetes Medications

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FLT3 plays a pivotal role in acute myeloid leukemia (AML), where its activation drives aberrant proliferation, differentiation, and apoptosis of hematopoietic cells. Current FLT3-targeted therapies, including inhibitors like Midostaurin and Gilteritinib, are limited by adverse effects and the emergence of resistance. This study analyzed datasets (GEO accession numbers GSE6891, GSE10358, GSE12662, GSE22056, and GSE17855), comparing 50 wild-type AML samples with 48 FLT3-associated samples to identify therapeutic targets and potential drugs for FLT3-mutated AML treatment. Approximately 200 hub genes were identified via STRING and

Cytoscape, with common pathways analyzed through Enrichr. The most frequently down-regulated genes included *CTNNB1*, *UBB*, *UBE21*, *BIRC5*, and *FOXO3*, while *JUN*, *EP300*, *TP53*, *FOS*, and *MAPK14* were the most up-regulated, primarily involved in CCKR and MAPK signaling pathways. Our findings suggest that JUN, IRS2, and YWHAE, along with their respective signaling pathways, could serve as potential therapeutic targets. Our virtual screening results revealed that Venetoclax, Itraconazole, Lutein, and Ponatinib exhibit a strong potential to bind with high affinity to the 14-3-3 ϵ protein (YWHAE), offering novel therapeutic avenues. Moreover, diabetes medications like insulin and metformin, as well as irbesartan (a hypertension drug), may be repurposed to benefit AML patients with FLT3 mutations. Our results highlight the therapeutic potential of repurposing metformin, insulin, and venetoclax for FLT3-mutated AML, offering a promising strategy to overcome resistance and improve patient outcomes. However, these results are preliminary and require further validation.

Keywords: Drug Repurposing, FLT3-Related AML, Diabetes Medications, Transcriptome

Is-9: Near-Infrared (NIR) Responsive Hydrogels as Emerging Wound Dressing: Why and How?

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One-third of the global mortality is related to bacterial infectious diseases, causing tremendous harm to human health. Skin plays a vital protective role in protecting the body from external harm, thus, it is of special importance to accelerate the treatment of damaged skin tissues especially bacterial infected ones. Benefiting from their favorable biocompatibility, distinctive physicochemical properties, and their ability to simulate the natural extracellular matrix, hydrogels are often used as excellent wound dressings. They have a three dimensional and porous structure and can absorb a large quantity of water, thus providing a moist environment to the wound environment. Due to wounds on the skin being often irregular in shape, conventional hydrogels cannot cover the wounds. Therefore, injectable counterparts have recently gained great attention because of their potential for filling an irregular wound. Recently, photothermal therapy (PTT) has attracted great interest in the treatment of bacteria-accompanied wounds. Under near-infrared (NIR) light irradiation, a high local temperature (>50 °C) generated by the NIR-active wound dressing or nanosystem kills bacteria. This is mainly due to physical damage (thermal destruction) to bacteria and on demand drug release when an antimicrobial drug is used. Here, we discuss recent advances on the development of novel photothermally active hydrogels in burn and infected wound healing. In addition, recent achievements at our research group on the design and fabrication of multifunctional hydrogels will be presented. To this aim, combination of PTT with gas delivery and chemodynamic therapy will be discussed in a wound healing process as well.

Is-10: Advances in Tissue Engineering and Cell Therapy for Corneal Diseases, with a Focus on Keratoconus

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Corneal diseases, particularly keratoconus, pose significant challenges in ophthalmology, often leading to visual impairment and requiring innovative therapeutic approaches. This presentation highlights the progress in tissue engineering and cell therapy for corneal regeneration, emphasizing foundational studies, animal models, and clinical applications, with a special focus on research conducted in Iran. Animal models have played a pivotal role in validating these approaches, showing improved corneal transparency and mechanical strength post-implantation. Additionally, stem cell therapies, particularly using limbal epithelial cells or mesenchymal stromal cells, have shown promise in restoring corneal epithelium and stroma in keratoconus patients. Iranian researchers have contributed significantly to this field, with studies reporting successful outcomes in both animal and early-phase human trials. The integration of tissue-engineered scaffolds with cell therapy offers a transformative pathway for treating corneal diseases, reducing reliance on donor tissues. This presentation will discuss these advancements, their translational potential, and future directions, underscoring Iran's role in pioneering affordable and accessible solutions for global ophthalmic care.

Keywords: Keratoconus, Tissue Engineering, Cell Therapy, Chitosan Scaffolds, Corneal Regeneration

Is-11: Metabolic Imaging in Cellular Organoid Quality Control: Innovative Strategies in Regenerative Medicine

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We utilized fluorescence lifetime imaging microscopy (FLIM) to non-invasively evaluate the metabolic states of human gingival and dental pulp-derived organoids through NADH lifetime analysis. Our approach identified distinct metabolic profiles characteristic of different cell sources and their combinations, while also revealing differential metabolic responses to bioprinting-associated stressors including UV exposure and thermal variations. The demonstrated capability of FLIM to assess organoid functionality and stress resilience establishes this technique as a valuable tool for quality assurance in 3D bioprinting applications, offering label-free metabolic evaluation prior to implantation.

Keywords: FLIM, NADH Metabolism, Organoid Quality Control, 3D Bioprinting, Dental Stem Cells, Non-Invasive Imaging

Is-12: Investigating the Molecular Mechanisms Underlying APOL1-Mediated Kidney Disease Employing A Unique Human Urine-Derived Podocyte Cellular Model

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Apolipoprotein L1 (APOL1) is a protein encoded by the APOL1 gene in humans. Genetic variants in APOL1 play a key role in the progression of kidney diseases. This effect is

primarily linked to two common protein-altering high risk variants, known as G1 and G2, which are found exclusively in individuals of African ancestry. In contrast, other populations predominantly express the wild-type (WT or G0) allele. Secretome analysis on a kidney injury associated arrays of urine samples from individuals with distinct APOL1 genotypes (G0/G0, G1/G1, G2/G2), with and without chronic kidney disease (CKD stages 2, 3, and 4) identified several upregulated proteins ADIPOQ, DPP4, LCN2, RETN and TNFRSF1A as potential CKD-associated cytokines. These proteins are implicated in key biological processes such as inflammation, metabolism and kidney function. Further analysis using a cytokine array revealed elevated levels of multiple proteins including APOA1, C5, CHI3L1, CRP, DPP4, CXCL1, GH1, IGFBP3, IL8, KLK4, LEP, MMP9, RBP4, SHBG, GC, and VEGFA. These factors are associated with heightened inflammation, endothelial dysfunction and fibrosis. Additionally, isolated SIX2-positive renal progenitor cells (UdRPCs) from the urine of G1/G1 and G2/G2 male individuals of African descent, as well as from a healthy G0/G0 European male, were differentiated into podocytes and stimulated with 100 μ M interferon-gamma (IFN- γ) for 24 and 48 hours. After 24 hours, significant upregulation of APOL1 along with a pronounced cytokine/chemokine response characterized by increased levels of CXCL1, CXCL9, CXCL10, CXCL11, CCL20, CSF2, ICAM1, IFNG, IL10, IL17A, IL18BP, IL31 and MIF. Metascape analysis revealed enrichment in biological pathways associated with inflammation and fibrosis, including ion transport regulation, immune system activation, prostaglandin signaling, Type II interferon signaling, and interleukin-mediated signaling. To mitigate IFN- γ -induced APOL1 upregulation, we treated the differentiated podocytes with the JAK inhibitor Baricitinib at concentrations of 0.1, 1, and 10 μ M. Pre-treatment with Baricitinib for 24 hours prior to IFN- γ stimulation resulted in a significant reduction in APOL1 mRNA and protein expression. Finally, we are currently reprogramming isolated G0/G0, G1/G2, G1/G1 and G2/G2 UdRPCs from patients with chronic kidney disease into induced pluripotent stem cells. Ultimately, these APOL1 iPSCs will be employed for investigating molecular mechanisms associated with APOL1 high-risk variants and their contribution to CKD and other kidney diseases.

Is-13: Genetically Modified Organoid: Platform to Target SWI/SNF Complex and Drug Screening

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The SWI/SNF chromatin-remodeling complex plays a pivotal role in regulating gene expression, and its dysregulation is frequently implicated in various malignancies. Among its subunits, ARID1A is one of the most commonly mutated components across solid tumors, including liver cancer. To investigate the functional consequences of ARID1A loss and establish a platform for targeted drug screening, we developed a genetically modified liver organoid model. Organoids were first isolated from primary liver tissue and cultured in a defined 3D environment to maintain physiological relevance. CRISPR/Cas9 genome editing was employed to knock out ARID1A,

and both Western blotting and RT-PCR confirmed successful gene disruption. Following genetic validation, we screened the ARID1A-deficient organoids using SAHA (vorinostat), a histone deacetylase inhibitor, to assess therapeutic vulnerability linked to SWI/SNF dysfunction. Our findings underscore the utility of organoid-based systems for modeling chromatin remodeling deficiencies and enable high fidelity preclinical drug testing. This platform not only enhances our understanding of epigenetic dependencies in liver cancer but also holds promise for identifying personalized therapeutic strategies targeting the SWI/SNF complex.

Keywords: Organoid, Epigenetic, Crispr-CAS9, Drug Screening

Is-14: Embryo Models and Mtor Signaling in Early Human Development

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Human peri-implantation development involves the precise coordination of lineage segregation, cavity formation, and communication with the maternal endometrium. Due to ethical and practical limitations in accessing in vivo human embryos, we employ human blastoids -stem cell-based models that recapitulate key features of early development. Using integrated transcriptomic and phosphoproteomic analyses, we identify mTOR signaling as a central regulator of cell fate balance. Modulation of mTOR activity alters lineage ratios, indicating a critical role in guiding early embryonic development. These findings highlight how nutrient-sensing pathways shape human embryogenesis and provide a framework for investigating the molecular causes of implantation failure. Human peri-implantation development involves the precise coordination of lineage segregation, cavity formation, and communication with the maternal endometrium. Due to ethical and practical limitations in accessing in vivo human embryos, we employ human blastoids -stem cell-based models that recapitulate key features of early development. Using integrated transcriptomic and phosphoproteomic analyses, we identify mTOR signaling as a central regulator of cell fate balance. Modulation of mTOR activity alters lineage ratios, indicating a critical role in guiding early embryonic development. These findings highlight how nutrient-sensing pathways shape human embryogenesis and provide a framework for investigating the molecular causes of implantation failure.

Is-15: Point of Care Testing, The Future and Market Analysis

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POCT is mainly characterized by proximity to the patient, quantitative or semi-quantitative single measurements, short turnaround time, no sample preparation, no pipetting, use of pre-made reagents, user-friendly dedicated analytical instruments and instant, result-deduced therapeutic action. All outpatient or ward personnel will be expected to be able to use these analyzers. No previous knowledge in sample analysis should

be required. POCT devices often employ biosensors. According to the IUPAC definition, a biosensor is an analytical device for the detection of analytes that combines a biological component with a physicochemical-detector component. This generally occurs through the use of miniaturized analysis systems, where biological components are immobilized on a solid-state surface, which, in turn, interacts with the analyte. These interactions may be detected by using either electrochemical or optical methods.

Type 1 – Qualitative strip-based POCT methods

Type 2 – So-called unit-use analyzers

Type 3 – So-called bench-top POCT analyzers

Type 4 – Hemostaseological coagulation analyzers

Type 5 – Continuous measurement with POCT systems

Type 6 – Molecular biology-based POCT devices to detect infectious agents

- North America was accounted highest revenue share more than 46% in 2023.

- Asia Pacific POCT market is registering at a CAGR of 12.38% from 2024 to 2034.

- Glucose monitoring products segment has captured highest revenue share 27% in 2023 valued at USD 8.91 billion in 2023.

- Lateral flow assays segment has accounted 36% revenue share in 2023.

- OTC testing products segment has held 59% revenue share in 2023.

- The biosensors segment is growing a CAGR of 9.2% during the forecast period.

- The pregnancy and fertility testing products segment is expected to reach at a 8.1% of CAGR from 2024 to 2034. The diagnostic centers segment is growing at a CAGR of 7.8% over the forecast period. The global point of care testing market size accounted for USD 39.64 billion in 2024, grew to USD 44.48 billion in 2025 and is predicted to surpass around USD 125.33 billion by 2034, representing a healthy CAGR of 12.20% between 2024 and 2034, market was valued at USD 36.6 Billion at the end of 2022 and is anticipated to exhibit growth of 5.8% in 2023. Sales grew at a CAGR of 6.2% between 2012 to 2022 contributes 40.0% revenue share to the global in-vitro diagnostics market valued at USD 91.2 Billion in 2022.

Is-16: Exploring the Fascinating Role of Astrocyte-Derived Exosomes: From Health to Disorder

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Understanding the mechanisms of cell-cell communication is essential for comprehending both physiological processes and pathological conditions. In recent decades, there has been a growing focus on the role of glial cells within the neuroscience community. Among these, astrocytes have emerged as vital contributors to the process of myelination, a function that was previously underestimated. Astrocyte cells play a crucial role in the brain's ecosystem, and their exosomes—tiny vesicles packed with proteins, lipids, and genetic material—are proving to be key players in both healthy brain function and various disorders. Discover how these remarkable little messengers transition from guardians of neural health to potential contributors in the development of neurological conditions. Our research

team has embarked on a novel investigation aimed at analyzing exosomes derived from glial cells, with a particular emphasis on those originating from healthy astrocytes in a disease model context. Our objective is to assess the potential of astrocyte-derived exosomes (Exo-Ast) to influence inflammatory pathways. Should this experimental system prove successful, the development of Exo-Ast may present a transformative approach to modifying disease progression. Prior to initiating extensive experimental protocols, we conducted a comprehensive review of the existing literature, which revealed that the primary role of astrocytes is intricately connected to exosome production. This finding implies that astrocytes can maintain their functionality through the regeneration of their exosomes. Unbiased by preconceived notions, we will present a fresh perspective on glial functions in relation to neurological disorders such as multiple sclerosis (MS) and Alzheimer's disease (AD).

Keywords: Exosome, Neurological Disorders, Astrocytes, Inflammation

Is-17: Enhancing Immune Cell Therapy in Hepatocellular Carcinoma via Pretreatment with All-trans Retinoic Acid

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Hepatocellular carcinoma (HCC) remains a major cause of cancer-related mortality worldwide, with limited therapeutic success in advanced stages. Immune cell therapy utilizing cytokine-induced killer (CIK) cells has emerged as a promising strategy due to its MHC-unrestricted cytotoxicity and favorable safety profile. However, enhancing the responsiveness of tumor cells to immune effectors remains a clinical challenge. All-trans retinoic acid (ATRA), a derivative of vitamin A, has demonstrated the ability to modulate tumor cell phenotypes and induce expression of stress ligands which are key elements in immune recognition. This study explores whether ATRA can sensitize HCC cells to immune-mediated cytotoxicity by up-regulating surface molecules recognized by CIK cells. Using a human HCC cell line (HepG2), we assessed the impact of ATRA pretreatment on cellular proliferation, surface ligand expression, and susceptibility to CIK cell-mediated lysis. The functional activity of expanded CIK cells was evaluated in vitro and further tested in a subcutaneous xenograft model in immunodeficient mice. Initial findings suggest that ATRA pretreatment reduces HCC cell proliferation and enhances immunogenic features associated with improved recognition by CIK cells. Co-culture experiments revealed synergistic effects on tumor cell apoptosis and cell cycle arrest. *In vivo* application of the combined approach indicated reduction in tumor volume and evidence of immune cell infiltration within the tumor site. These results highlight the potential of pharmacological priming strategies, such as ATRA treatment, to enhance the therapeutic efficacy of CIK-based immune cell therapy. By promoting immune susceptibility of tumor cells, this approach may offer a complementary modality to improve clinical outcomes in HCC. Further mechanistic studies and translational assessments are warranted to refine this combination therapy for future application.

Keywords: Hepatocellular Carcinoma, Cytokine-Induced Killer Cells, Retinoic Acid, Immunotherapy, Tumor Sensitization,

Differentiation Therapy

Is-18: Building A Coordinated Ecosystem for Precision Oncology in Iran**Mowla SJ**

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Each year, over 190,000 new cancer cases are registered in Iran—a number that continues to rise. Addressing this growing burden requires a systematic model for cancer diagnosis and treatment tailored to the national context. To this end, the Cancer Genomics Holding and its affiliated startups have initiated a comprehensive effort to map Iran's cancer ecosystem and foster synergy among its key components. This initiative aims to integrate research, clinical translation, and management of the 20 most prevalent cancers in Iran. Core objectives include institutionalizing molecular diagnostics and precision oncology based on the latest international and national guidelines, localizing and harmonizing comprehensive diagnostic assays, and coordinating the development of targeted therapies. Additionally, the launch of the "CancerMed" information platform provides a centralized resource for cancer-specific data, facilitating patient referrals to physicians, diagnostic laboratories, and pharmaceutical providers. Through this ecosystem-driven approach, the Holding seeks to transform cancer care in Iran by bridging scientific innovation with clinical practice.

Is-19: Artificial Intelligence in Medicine: Enhancing Diagnosis, Treatment, and Patient Care**Abolghasemi Dehaqani MR**

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Artificial Intelligence (AI) is revolutionizing healthcare by improving accuracy, efficiency, and personalization in medical practice. AI-powered tools assist in early disease detection through advanced imaging analysis (e.g., identifying tumors in X-rays or MRIs), predicting patient risks using electronic health records, and optimizing treatment plans with machine learning. Natural language processing (NLP) helps extract insights from medical literature and patient notes, while robotic surgery enhances precision in operations. Additionally, AI accelerates drug discovery by analyzing vast datasets for potential therapies. Despite challenges like data privacy and ethical concerns, AI's integration into medicine promises faster diagnoses, reduced costs, and better patient outcomes—ushering in a new era of smart healthcare.

Is-20: Translational Insight into Chemotherapeutic Nanoparticles for Cancer: Exosome Therapy or Cell Therapy?**Niknejad H**

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Due to reducing unexpected side effects of chemotherapeutic

drugs and improving clinical outcomes, targeted drug delivery is a research interest in treatment of cancer. Chemotherapeutics loaded stem cells and alternatively stem cell derived exosome as cargo of anti-cancer drugs are two methods of choice in the field. Inherent anti-cancer characteristics like induction of apoptosis, inhibition of angiogenesis, and cell-cycle arrest in neoplastic cells are some advantages of stem cells. However, biosafety problems in transplantation of living cells make exosomes superior to stem cells. From the efficiency point of view, we compared exosome therapy with stem cell therapy in ex-vivo cell culture and tumor assay in preclinical model of cancer in nude mice from gene to protein expression level. Amniotic epithelial stem cells primed with paclitaxel nanoparticles and their exosomes were used in experiments. Several serial concentrations were assessed to optimize the loading and release efficiency of stem cells and their exosomes. The results showed that stem cells were resistant to nano-paclitaxel. In vitro and animal model evaluations exhibited both loaded stem cells and exosomes suppressed cancer cell lines proliferation, induced apoptosis in tumor cells, inhibited angiogenesis and decreased tumor size; but stem cells were more efficient than exosomes. We conclude from the results that in addition to bypassing some challenges such as biosafety, therapeutic benefit is a critical determinant in decision-making between two paths in translational medicine: stem cell therapy or exosome therapy.

Is-21: Contribution of microRNAs to The Regulation of Pluripotency**Moradi Sh**

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Embryonic stem cells (ESCs) derived from the inner cell mass (ICM) possess unlimited self-renewal capacity while retaining multi-lineage differentiation potential. The transition from ICM to ESCs involves dynamic regulatory pathways, though the role of non-coding RNAs remains poorly understood. Here, we investigate the contribution of microRNAs (miRNAs) in ESC formation and ground-state pluripotency—a state maintained through repression of differentiation pathways. Using small-RNA sequencing, we characterize time-dependent miRNA expression dynamics during ICM outgrowth and identify waves of miRNA transcription, with significant contributions from the imprinted *Dlk1-Dio3* locus. Functional studies reveal that *Dlk1-Dio3*-embedded miRNAs (miR-541-5p, miR-410-3p, and miR-381-3p), miR-183-5p, miR-363-3p, and miR-302b-3p promote ESC formation, while miR-212-5p and let-7d-3p inhibit it. Moreover, ground-state pluripotency is associated with a distinct miRNA signature, predominantly encoded by the *Dlk1-Dio3* locus, which enhances self-renewal and suppresses differentiation. Furthermore, the ESC-enriched miRNAs miR-30d-5p and miR-148a-3p drive the generation of induced pluripotent stem (iPS) cells. Collectively, our findings provide mechanistic insights into the critical roles of miRNAs in ESC derivation and the maintenance of ground-state pluripotency.

Is-22: Application of Metabolic Models for Understanding Cell Differentiation**Marashi SA**

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In recent years, metabolic network modeling of stem cells using genome-scale reconstructions and flux balance methods has become a central tool for deciphering the key pathways that govern their metabolism; integrating transcriptomic and metabolomic data not only uncovers metabolic rewirings and critical regulatory nodes during differentiation, but also enhances our ability to predict cellular responses to genetic and environmental perturbations. Current models show that stem cells in their early state predominantly rely on glycolysis for energy supply, while in the course of differentiation, they shift markedly toward oxidative phosphorylation. These metabolic shifts can guide the targeted design of optimized protocols for differentiation, proliferation, and reprogramming. Looking ahead, the development of dynamic flux balance analysis and multi-omics models to simulate temporal metabolic changes during differentiation, the integration of single-cell omics data to map functional heterogeneity within cell populations, and the application of machine learning methods to optimize modeling parameters and predict complex cellular behaviors—all promise to substantially improve strategies for controlling stem cell differentiation and expansion.

Is-23: Sulfated Alginate-Based Scaffolds for Engineering of Soft Tissues

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Background: Design and synthesis of sulfated alginate-based engineered constructs including hydrogels, films, and nanofibrous mats are of interest as available, renewable and low-cost biomaterials for engineering of different soft tissues. These constructs could trigger main activities of the cells including cell proliferation, migration, differentiation and also tissue repair. In this regard, our primary focus centers on unraveling the pivotal role of the sulfated alginate as a constituent of scaffolds on cell and tissue behaviors.

Materials and Methods: The sulfated alginate solely or in combination with other materials has been employed to be evaluated in point of its role on cell activities of different cells including fibroblasts, endothelial cells, macrophages, mesenchymal stem cells, islets and etc. For this aim, sulfated alginate was physically or chemically modified by calcium cations, isocyanate-based or/and vinyl-functionalized polyurethane, methacrylated chitosan, and carbodiimide chemistry. All of the sulfated alginate-based constructs including hydrogels, nanofibrous mats, and microparticles were first both physically and chemically characterized by FTIR, NMR, CHNS elemental analysis, EDX mapping, and etc. After that, different *in vitro* analyses including cell viability, scratch assay, cell adhesion, hemocompatibility, protein adsorption and were performed on resulting engineered constructs. Finally, different *in vivo* experiments were performed in accordance with the guidelines established by the acquired centers, and histological and immunohistological aspects of the healed tissues were studied.

Results: Appearance of carboxylate, sulfate and methacrylate

functional groups at 1650-1680 cm⁻¹, 1260-1270 cm⁻¹, and 1700-1730 cm⁻¹ confirmed chemical structure of sulfated alginate and its derivatives. Further characterization by NMR spectroscopy and elemental analysis confirmed the successful sulfation, methacrylation, and urea formation in chemical structure of sulfated alginate and final engineered constructs by appearance of the characteristic peaks at 5.8-6.2 ppm and 4.5-4.7 ppm. The results of both indirect and direct MTT assays showed appropriate cytocompatibility for all constructs. In addition, the results of histopathological analyses of engineered constructs as wound dressing, cell carrier and tough hydrogel well showed proper biocompatibility against control samples.

Conclusion: The appearance of deterministic bands, peaks, and required elements and functional groups in chemical structure of these constructs confirmed the chemical structure of proposed biomolecules by abovementioned techniques. The microstructure of the engineered constructs was studied by microscopic instruments like SEM analysis, and the nanofibrous or microporous structure of each construct was approved. Based on the *in vitro* cytotoxicity experiments, the scaffolds not only showed no cytotoxicity, but the cell growth and migration also dramatically increased by increasing the sulfated alginate content. The ability of prepared constructs as hydrogel to promote wound healing process in diabetic animals, as nanofibrous mats to be used as functional tissue-engineered small-diameter vascular grafts, as double network hydrogel to mitigate fibrosis for long-term glycemic control in diabetic mice, and finally, as microparticle to promote articular cartilage tissue regeneration in rabbits revealed significant role of sulfated alginate as a bioactive semi-synthetic polysaccharide for regeneration of soft tissues.

Keywords: Sulfated Alginate, Tissue Engineering, Soft Tissues

Is-24: Enhanced Alveolar Bone Regeneration Induced by Hemostatic, Osteogenic and Angiogenic Nano-Biomaterials: Progress, Challenges and Future Perspectives

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Persistent hemorrhage and alveolar bone resorption following tooth extraction complicating subsequent dental implant interventions highlighting the necessity of developing scaffolds with triple hemostatic, osteogenic and angiogenic properties. Here in a comprehensive study was done to engineered scaffolds from modified biomaterials and nanoparticles with simultaneous hemostatic, osteogenic, and angiogenic capabilities for *in-situ* alveolar bone regeneration. The *in vitro* hemostatic assays result like blood clotting index (BCI), red blood cell adhesion, and platelet aggregation (LDH assay) and dense fibrin clot formation were approved high hemostatic ability of engineered scaffolds. The *in vitro* cellular assessments demonstrated that the biomaterial encompassing blood clots dramatically elevated the expression of bone-associated RUNX2 and OCN proteins, boosted the activity of alkaline phosphatase (ALP), and facilitated the deposition of mineralized extracellular matrix of bone marrow stem cells. *In vivo* experiments using a rat mandibular tooth extraction model demonstrated a nearly two-fold re-

duction in bleeding time and blood loss compared to control groups. Substantial in-situ alveolar bone regeneration was observed in rats treated with In-situ bone regeneration evaluation in rate received engineered scaffolds through CBCT and Micro-CT imaging and histological analyses indicated that the application of these engineered scaffolds led to a notable improvement in osteogenesis, achieving a BV/TV (bone volume/tissue volume) of 85%, being significantly higher than commercial Gelita® (50%) and control group (45%) ($P < 0.01$). The highly clot formation capability through platelet activation and coagulation cascade acceleration along with the incorporation of osteogenic bioactive ingredients and angiogenic compounds into the tailored scaffold allow for the ingrowth and proliferation of stem cells, thus facilitating osteogenic differentiation and can serves as an effective treatment strategy for the clinical management of post-extraction wounds.

Keywords: Alveolar Bone Regeneration, Hemostatic Sponge, Nanocomposite, Angiogenic Biomaterials, Bone Marrow Stem Cell Regeneration

Is-25: Monkey Cloning, Chimera, and Embryo Model

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A formal demonstration that mammalian pluripotent stem cells possess preimplantation embryonic cell-like (naïve) pluripotency is the generation of chimeric animals through early embryo complementation with homologous cells. Whereas such naïve pluripotency has been well demonstrated in rodents, poor chimerism has been achieved in other species including non-human primate due to the inability of the donor cells to match the developmental state of the host embryos. Here, we have systematically tested various culture conditions for establishing monkey naïve embryonic stem cells and optimized the procedures for chimeric embryo culture. This approach generated an aborted fetus and a live chimeric monkey with high donor cell contribution. A stringent characterization pipeline demonstrated that donor cells efficiently (up to 90%) were incorporated into various tissues (including the gonads and placenta) of the chimeric monkeys. Using monkey naïve ESCs, we have for the first time reported the generation of monkey blastoids, and these blastoids can be cultured in vitro to D17 with gastrulation and three germ layer differentiation. Our results have major implications for the study of primate naïve pluripotency and genetic engineering of non-human primates.

Is-26: Immunomodulatory Biomaterials For Treatment & Regeneration

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Modern immunotherapies save lives but are often slow, costly, and hard to translate to solid tumors and aging immune systems. This talk presents a broadly applicable strategy: biomaterials that train the immune system in place. By combining local delivery of immune cues with control over the mechanical environment, these materials create temporary “learning nich-

es” that recruit, activate, and program immune cells where they are needed—without extensive cell manipulation or systemic toxicity. I’ll outline core design principles, share representative preclinical outcomes, and discuss how this approach can complement existing vaccines and cell therapies. Beyond oncology, the same concepts point to new directions for improving vaccine responses in older adults, resolving chronic inflammation, and accelerating tissue repair. Together, these adaptive biomaterials illustrate a path toward faster, safer, and more durable immune interventions across diseases.

Is-27: Immuno Virotherapy in Glioblastoma

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Glioblastoma (GBM) remains one of the most aggressive brain tumors, requiring innovative therapeutic strategies. In this work, we examined the antitumor properties of Onco-VV-TT, an engineered oncolytic vaccinia virus, and evaluated whether natural killer (NK) cell therapy could potentiate its effects. Human fibroblast (HFF) and U251 glioblastoma cells were used to characterize viral replication and cytotoxicity through a panel of assays, including MTS viability, colony formation, migration studies, flow cytometry, 3D spheroid cultures, and quantitative PCR. For *in vivo* validation, both immunocompetent and nude xenograft mouse models were employed. Mice received intratumoral injections of Onco-VV-TT either alone or in combination with NK cells, and treatment outcomes were monitored by measuring tumor growth, overall survival, systemic toxicity markers, and immune responses. Tumor sections were further examined histologically. Onco-VV-TT replicated efficiently in U251 cells and induced substantial cell death, with spheroid assays confirming reduced tumor cell viability and impaired growth in 3D cultures. In animal models, the virus suppressed tumor progression, and its combination with NK cells provided even greater therapeutic benefit. Importantly, biochemical, hematological, and immunological assessments showed limited off-target toxicity. Histopathology demonstrated enhanced necrosis and apoptosis within tumor tissues, accompanied by decreased expression of angiogenesis- and stemness-associated markers. These results highlight the dual action of Onco-VV-TT, direct tumor lysis and immune activation, and underscore

the added value of NK cell therapy. Together, this combinatorial strategy represents a promising candidate for future GBM treatment and warrants further preclinical and clinical exploration.

Is-28: Microfluidic Systems for Cell Biology and Translation into Practice

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Microfluidics, a technology characterized by the engineered manipulation of fluids at the microscale, has shown considerable promise in point-of-care diagnostics and clinical research. By offering precise control over the cellular microenvironment, microfluidic platforms are becoming valuable tools for cell biologists to further their understanding of complex biological systems. The miniaturization of macroscopic systems and the ability for massive parallel processing make microfluidic chips particularly well-suited for high-throughput biological experiments. These chips can enable diverse applications, including particle/cell sorting, single cell analysis, digital PCR, drug screening, etc. Over the past decade, my group has developed several microfluidic systems, which are translated into practice. In this seminar, I will highlight our advances in rare cell and exosome sorting for liquid biopsy, organ-on-chip technologies for drug screening and integrated tools for CRISPR gene editing.

Is-29: Molecular Traffic in Stem Cells: Decision Making Fine Tuned

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Is-30: Development of Polymeric Gene Delivery Carriers: Horizons in Gene Therapy and mRNA Vaccination

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Is-31: Removal of Residual Undifferentiated Cells from Pluripotent Stem Cell Derived Cardiomyocytes by Small Molecules

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Is-32: Cell therapy in pediatrics: clinical trial experiences

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Oral Presentation

Os-1: MicroRNA-363-3p Promotes Mouse Embryonic Stem Cell Formation by Modulating Autophagy through Stx17 Targeting

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Objective: MicroRNAs (miRNAs) are critical regulators of pluripotency, but the role of miR-363-3p during the derivation of mouse embryonic stem cells (mESCs) remains poorly understood. While autophagy is known to influence stem cell homeostasis, its interplay with pluripotency pathways is unclear. This study reveals miR-363-3p as a dual-function modulator that enhances pluripotency while suppressing autophagy, offering new mechanistic insights into stem cell regulation.

Materials and Methods: We combined bioinformatics and experimental approaches to identify Syntaxin 17 (Stx17)—a key autophagy regulator—as a target of miR-363-3p. The effects of miR-363-3p overexpression in mESCs were assessed using qRT-PCR, Western blot, and immunocytochemistry (LC3-II/I, p62). Pluripotency was evaluated via transcriptomics (RNA-Seq), principal component analysis (PCA), and differentiation assays. In vivo functionality was tested through chimeric mouse embryos generated from GFP-labeled miR-363-3p-treated mESCs. Mechanistic validation employed dual-luciferase reporter assays targeting the Stx17 3'UTR.

Results: miR-363-3p overexpression significantly downregulated Stx17, impairing autophagic flux (reduced LC3-I/II conversion, p62 accumulation). By suppressing autophagy, miR-363-3p promoted the self-renewal and pluripotency of mESCs without compromising their differentiation potential, upregulating core pluripotency factors (Oct4, Nanog, Sox2). Notably, chimera contribution assays demonstrated extensive GFP⁺ cell integration into fetal tissues, confirming functional pluripotency. Luciferase assays and complementary functional analyses confirmed direct miR-363-3p binding to the Stx17 3'UTR, linking autophagy inhibition to pluripotency enhancement.

Conclusion: Our study establishes miR-363-3p as a novel driver of pluripotency that fine-tunes stemness by suppressing Stx17-mediated autophagy. These findings underscore the crosstalk between autophagy and pluripotency, with implications for cellular reprogramming.

Keywords: RNAi, Gene regulation, Embryonic Stem Cells, miR-363, Autophagy

Os-2: Development of a Colorimetric Y-shaped DNA Biosensor for miR-21-5p Detection in Cancer

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Objective: MicroRNAs (miRNAs) regulate gene expression and are often dysregulated in cancer, with miR-21-5p serving as

a key biomarker. We developed a simple colorimetric biosensor using gold nanoparticles (AuNPs) and a Y-shaped DNA probe for sensitive detection of miR-21-5p.

Materials and Methods: AuNPs (~20 nm) were synthesized via citrate reduction and conjugated with an NH₂-modified Y-shaped DNA probe complementary to miR-21. For detection, miR-21 (0–20 μM) was incubated with the probe-bound AuNPs (2 μM, 37°C, 30 min), triggering probe displacement and salt-induced AuNP aggregation. This caused a visible color shift (red → blue), quantified by UV-vis spectroscopy or DLS/TEM for size validation.

Results: UV-vis analysis showed the AuNPs' 525 nm peak dropping, while a new 650 nm aggregation peak appeared as miR-21 concentration increased. The A₆₅₀/A₅₂₅ ratio yielded a linear correlation (R² = 0.98) from 0.1 to 10 μM miR-21, with a 50 nM detection limit at S/N=3. DLS confirmed the formation of large aggregates (>200 nm) in miR-21-treated samples, while TEM images visualized the transition from dispersed AuNPs to clustered structures upon miR-21 binding. The assay showed high specificity for miR-21, with negligible signal changes observed for control miRNAs (miR-16, miR-155) or single-base mismatches. The presence of human serum (up to 10%) did not interfere with detection, confirming robustness in complex biological matrices.

Conclusion: The Y-shaped DNA-AuNP biosensor offers a sensitive, rapid, and visual method for miR-21 detection, with potential as a versatile platform for miRNA-based liquid biopsies and point-of-care cancer diagnostics.

Keywords: Biomarker, Early Detection, Gold Nanoparticles, Nanobiosensor

Os-3: Clinical Assessment of Exosome Eye Drops Derived from Wharton's Jelly Mesenchymal Stem Cells for Dry Eye Disease

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Objective: Exosomes derived from Wharton's Jelly Mesenchymal Stem Cells (WJ-MSCs) are promising for regenerative therapies due to their immunomodulatory and reparative properties. This study assessed the safety and efficacy of WJ-MSC-derived exosome eye drops in patients with moderate to severe Dry Eye Disease (DED) over three months.

Materials and Methods: Fifteen patients (30 eyes) with DED were enrolled. In addition to their standard treatments, participants instilled exosome eye drops every six hours for three months. Clinical parameters were assessed before and after treatment, including Uncorrected and Best Corrected Visual Acuity (UCVA, BCVA), intraocular pressure, contrast sensitivity, Tear Meniscus Height (TMH), non-invasive tear Break-up Time (niBUT), Schirmer test, Ocular Surface Disease Index (OSDI), Ocular Surface Inflammatory Risk Evaluation (OSIE), meibography, ocular redness grading, and specular microscopy for corneal endothelial metrics.

Results: No adverse events were observed, confirming the treatment's safety. Significant improvements were noted across several parameters. TMH increased from 16.6 ± 2.3 μm to 23.2

$\pm 3.3 \mu\text{m}$; niBUT improved from $4.22 \pm 2.99 \text{ s}$ to $6.79 \pm 2.93 \text{ s}$; and Schirmer scores rose from $5.53 \pm 4.33 \text{ mm}$ to $8.30 \pm 3.46 \text{ mm}$. OSDI scores declined from 33.11 ± 14.50 to 20.98 ± 11.69 , indicating reduced symptom severity. Visual acuity and contrast sensitivity also improved, with no changes in corneal endothelial cell density or thickness.

Conclusion: Topical application of WJ-MSC-derived exosome eye drops was safe and well tolerated, resulting in significant symptomatic and clinical improvement in DED patients. These findings support exosome therapy as an effective, cell-free approach for managing ocular surface disease. Larger, controlled trials are needed to further optimize dosing and validate efficacy.

Keywords: Exosomes, Wharton's Jelly Mesenchymal Stem Cells, Dry eye disease, Ocular surface therapy, Cell-Free Regenerative Medicine

Os-4: Design and Development of a Chitosan Hydrogel with Natural Antioxidants to Induce Fibroblast Differentiation of Mesenchymal Stem Cells for Skin Tissue Engineering

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Objective: The use of hydrogel scaffolds is highly relevant in regenerative medicine and skin tissue engineering. This study investigates the expression of the Collagen gene in Mesenchymal Stem Cells (MSCs) differentiated into Fibroblasts in the presence of Chitosan hydrogel (CTS) and the antioxidant Alpha-tocopherol (α -toco).

Materials and Methods: CTS hydrogel containing Alpha-tocopherol was synthesized and characterized using Scanning Electron Microscopy (SEM). The MTT assay assessed the non-toxicity and biocompatibility of Adipose Mesenchymal Stem Cells (AMSCs) in 24 hours. Real-time PCR was employed to evaluate Collagen type I gene expression to confirm fibroblast differentiation.

Results: SEM images of the hydrogel revealed a desirable morphology with a porous structure. MTT assay results indicated that AMSCs interacted with the hydrogel without toxicity. Real-time PCR showed significant increases in differentiation markers of AMSCs in CTS hydrogel containing Alpha-tocopherol compared to the control ($p < 0.001$).

Conclusion: Alpha-tocopherol, a natural antioxidant combined with CTS hydrogel, can enhance the growth and differentiation of AMSCs into Fibroblasts and is a promising candidate for skin tissue engineering.

Keywords: Chitosan, Hydrogel, Alpha-tocopherol, Mesenchymal Stem Cells, Fibroblast Differentiation

Os-5: Evaluation of Vitronectin N as an Extracellular Matrix for GMP-Compatible Maintenance and Expansion of Human Embryonic Stem Cells

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Objective: A defined, Xeno-free, and cost-effective extracellular matrix (ECM) is essential for the reproducible culture of human embryonic stem cells (hESCs). This study evaluates Vitronectin type-N (VTN-N) as a consistent, Xeno-free, and defined alternative ECM for GMP-compliant hESCs manufacturing.

Materials and Methods: RH6 hESCs were cultured on VTN-N, Matrigel, and feeder cells (controls). Cell adhesion and viability were assessed using adherence assays and cell counting. Proliferation was evaluated via doubling time calculation, Ki-67 immunocytochemistry, and cell cycle analysis. Pluripotency was assessed via qRT-PCR and immunostaining for OCT4 and NANOG. Karyotyping was performed after several passages on VTN-N.

Results: No significant differences were observed between VTN-N and Matrigel in terms of cell adhesion and viability ($p \geq 0.05$). While cells on Matrigel showed faster initial proliferation, long-term culture on VTN-N enhanced the G2/S phase population (~56%), indicating improved proliferative capacity. Both ECMs maintained pluripotency marker expression, with no chromosomal abnormalities observed in cells passaged 14 times on VTN-N.

Conclusion: VTN-N offers an effective and defined ECM for long-term, GMP-compliant culture of hESCs, supporting cell growth, proliferation, and pluripotency. This ECM alternative could contribute to advancing hESC-based therapies and manufacturing processes.

Keywords: Vitronectin-N, Embryonic Stem Cells, Xeno-Free, Extracellular Matrix, GMP

Os-6: Systematic Review of Long Non-coding RNAs (lncRNAs) in the Epigenetic Regulation of Pluripotency: Implications for Stem Cell Therapy

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Objective: Long non-coding RNAs (lncRNAs) play a significant role in regulating stem cell pluripotency and differentiation. While their transcriptional roles are well established, their impact on the epigenetic regulation of pluripotency, particularly through chromatin-modifying complexes, remains insufficiently understood. This review synthesizes current evidence on the role of lncRNAs in epigenetic regulation and their implications for stem cell therapy.

Materials and Methods: A systematic PubMed search was conducted for studies published from January 2015 to December 2024 using the query: ("long noncoding RNA"[Title/

Abstract] OR "lncRNA"[Title/Abstract]) AND ("stem cell"[Title/Abstract] OR "pluripotency"[Title/Abstract])) NOT ("cancer"[Title/Abstract] OR "tumor"[Title/Abstract]). Studies investigating lncRNA-mediated epigenetic regulation in human or mouse stem cells were screened, and relevant data were extracted.

Results: Of 527 records, 24 studies met inclusion criteria, identifying 40 lncRNAs involved in the epigenetic regulation of pluripotency. These were categorized into seven functional groups:

1. Polycomb recruitment (PRC2/PRC1) to silence pluripotency genes (6 lncRNAs, e.g., HOTAIR)
2. DNA methylation/demethylation at promoter regions (3 lncRNAs, e.g., TARID)
3. Modulation of Wnt/ β -catenin and TGF- β /Smad signaling (4 lncRNAs, e.g., H19)
4. miRNA sponging (4 lncRNAs, e.g., Linc-RoR)
5. Chromatin scaffold or nuclear architecture formation (3 lncRNAs, e.g., NEAT1)
6. DNA repair and genomic stability maintenance (1 lncRNA, CIRKIL)
7. Angiogenesis and tissue regeneration (2 lncRNAs, e.g., KLF3-AS1)

Thirteen lncRNAs were implicated in stem cell models (e.g., hESCs, iPSCs). Notably, lncRNAs such as Platr10 and Linc-RoR were critical for maintaining pluripotency, facilitating reprogramming, and regulating key genes like OCT4 and NANOG.

Conclusion: lncRNAs are versatile regulators of pluripotency, serving as scaffolds for chromatin-modifying complexes and influencing pluripotent states. Their diverse mechanisms highlight their potential as targets for enhancing iPSC reprogramming and stability, though more standardized and context-specific validation is necessary.

Keywords: lncRNAs, Stem Cells, Pluripotency, Epigenetics

Os-7: Non-Invasive Harvesting of Retinal Pigment Epithelium (RPE) Monolayer Cell Sheet Using Dual-Responsive Co-Polymeric Substrate Aiming for Clinical Application

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Objective: Damage to the retinal pigment epithelium (RPE) is a leading cause of vision loss in several retinal diseases. This study introduces an innovative, scaffold-free method for harvesting viable RPE monolayers using dual-responsive co-polymeric substrates, providing a non-invasive approach for cell sheet engineering.

Materials and Methods: A dual-responsive substrate was synthesized by grafting thermo-responsive poly N-isopropylacrylamide and saccharide-responsive poly 3-acrylamidophenylboronic acid onto tissue culture plates via RAFT polymerization. This substrate enables rapid, non-invasive detachment of intact RPE monolayers without the need for enzymes or biodegradable scaffolds. Characterization techniques, including atomic force microscopy, Fourier transform infrared spectroscopy, and NMR, were employed to verify the substrate's properties. RPE cells were cultured on the substrate and tested for cell markers (ZO1, MITF, Bestrophin) and polarization integrity.

Results: The dual-responsive substrate successfully facilitated

the detachment of RPE cell sheets, maintaining cellular markers and apico-basal polarization. In vivo transplantation of a 1×1 mm RPE sheet into Royal College of Surgeons rats showed integration of the transplanted layer with the retina and enhanced outer nuclear layer thickness after eight weeks, supporting the functional integrity of the cells.

Conclusion: This study presents the first scaffold-free RPE harvesting technique in Iran, utilizing dual-responsive substrates. This non-invasive approach holds great potential for future clinical applications in retinal therapies, particularly in treating age-related macular degeneration.

Keywords: Tissue Engineering, Retina, Stimuli-responsive Materials, Clinical Therapy

Os-8: Genistein-loaded Extracellular Vesicles Enhance Osteogenic Activity of Mesenchymal Stem Cells

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Objective: Osteoporosis is a prevalent skeletal disorder marked by bone mass reduction. Phytoestrogens, such as genistein, are known for promoting osteogenesis. This study investigates the synergistic effect of genistein-loaded extracellular vesicles (EVs) derived from mesenchymal stem cells (MSCs) on osteogenic differentiation, offering a novel therapeutic approach for bone regeneration.

Materials and Methods: Rat bone marrow-derived MSCs were cultured, and EVs were isolated using centrifugation followed by filtration and concentration. The EVs were characterized using scanning electron microscopy (SEM), dynamic light scattering (DLS), and Western blotting. The optimal concentration for drug loading was determined via MTS assay. Osteogenic differentiation was assessed using alkaline phosphatase (ALP) activity, Alizarin Red staining for mineralization, and real-time PCR analysis of osteogenic markers.

Results: Genistein-loaded EVs exhibited enhanced osteogenic differentiation, with increased ALP activity, mineralization, and upregulation of osteogenic genes like Runx2 and OCN. SEM confirmed the characteristic morphology of EVs, and molecular analysis indicated the presence of surface markers (CD63, CD81). The EV+Gen group showed superior osteogenic potential compared to the control and genistein-only groups.

Conclusion: The combination of genistein with MSC-derived EVs presents a promising approach for enhancing osteogenesis, offering a cell-free therapeutic strategy for osteoporosis treatment.

Keywords: MSC-EVs, Genistein, Osteogenesis, Osteoporosis

Os-9: Evaluation and Comparison of Viability and Persistence between Two Types of CD19-CAR T Cells Produced by Conventional and Fast Culture Conditions

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Objective: Chimeric Antigen Receptor (CAR) T cell therapy is a transformative treatment for various malignancies, involving the genetic engineering of a patient's T cells to selectively target tumor-associated antigens. Conventional CAR T cell manufacturing typically takes 2 to 3 weeks due to complex steps such as T cell activation, expansion, and strict quality control. Recent advances have enabled accelerated production protocols, reducing the process to about 48–72 hours by minimizing or skipping the ex vivo expansion phase. These faster methods improve patient access, lower manufacturing costs, and may generate less differentiated T cell populations with better long-term efficacy.

Materials and Methods: In this study, CAR T cells were produced using two protocols: a conventional 12-day method (CT-CARaCell19) and an accelerated 4-day approach (FT-CARaCell19). Cells from both groups were co-cultured with Raji target cells at an effector-to-target (E:T) ratio of 1:1 for 7, 14, and 21 days. After each period, cells were stained with fluorescent antibodies for markers of memory phenotype (CD45RA, CCR7), exhaustion (PD-1, TIM-3), and apoptosis (Annexin V, 7-AAD). Flow cytometry was performed using a BD FACS-Canto II system, and data were analyzed with FlowJo software (v10.8). Experiments were conducted with cells from three healthy donors.

Results: The results showed that FT-CARaCell19 produced a higher proportion of less differentiated memory T cells. These cells exhibited better functional performance during co-culture with Raji cells, with delayed exhaustion and improved fitness. The accelerated protocol also yielded a higher percentage of viable CAR T cells than the conventional 12-day process, indicating superior cellular quality, resilience, and durability.

Conclusion: Less differentiated memory T cells from the fast protocol demonstrated prolonged proliferation, delayed exhaustion, and enhanced survival, likely due to their stem-like and central memory phenotypes. These traits support sustained proliferation and persistence, potentially improving therapeutic durability and clinical outcomes.

Keywords: CAR T cell therapy, Blood cancer, Memory phenotype, Exhaustion, Apoptosis

Os-10: Combination Therapy with Pirfenidone and Mesenchymal Stem Cell-Conditioned Medium Promotes Uterine Regeneration and Reduces Fibrosis in a Mouse Model of Intrauterine Adhesions

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Objective: Intrauterine adhesions (IUA), often caused by endometrial injury or infection, are a major contributor to infertility,

recurrent pregnancy loss, and menstrual irregularities. Current treatments, including adhesiolysis and hormonal therapy, have limited effectiveness, emphasizing the need for improved therapeutic strategies. This study investigated the therapeutic potential of pirfenidone, an FDA-approved anti-fibrotic and anti-inflammatory drug, either alone or in combination with mesenchymal stem cell-conditioned medium (MSC-CM) in a murine IUA model.

Materials and Methods: Mesenchymal stem cells (MSCs) were isolated from human umbilical cords, characterized, and used to produce conditioned medium. IUAs were induced in NMRI mice through mechanical endometrial injury. The mice (n=25) were divided into seven groups: normal, sham, IUAs + PBS, IUAs + CM, IUAs + pirfenidone (100 or 200 mg/kg), and IUAs + pirfenidone (100 mg/kg) + CM. Treatments began five days after injury and continued for one week. Uterine repair was assessed using H&E and Masson's trichrome staining, α SMA immunohistochemistry, analysis of fibrosis-related gene expression (COL1, α SMA, SMAD, TGF- β), pregnancy outcomes, and in vitro scratch assays to assess cell migration.

Results: Pirfenidone improved endometrial thickness, gland number, vascularization, and reduced fibrosis, with enhanced effects when combined with MSC-CM. Fibrotic gene expression was downregulated, and fertility outcomes improved in treated groups. MSC-CM alone supported regeneration and cell migration, while combination therapy produced the most significant benefits.

Conclusion: This is the first study to demonstrate pirfenidone's effectiveness in treating IUAs. Its combination with MSC-CM showed synergistic regenerative effects and presents a promising approach to restore endometrial function and fertility with reduced drug dosage.

Keywords: Intrauterine adhesions, Mesenchymal stem cells, Conditioned medium, Pirfenidone, Regenerative therapy

Os-11: Stem Cell Therapy in Endometriosis: A Novel and Multifaceted Therapeutic Approach

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Objective: Endometriosis is a chronic, estrogen-dependent inflammatory disorder characterized by the presence of endometrial-like tissue outside the uterine cavity. It affects up to 10% of women of reproductive age and is associated with chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility. Current treatments, including hormonal therapies and surgical intervention, are often limited by recurrence, incomplete symptom relief, and side effects. In recent years, stem cell-based therapies—especially those involving mesenchymal stem cells (MSCs)—have emerged as promising alternatives due to their regenerative, immunomodulatory, and anti-inflammatory properties.

Materials and Methods: This study is based on a systematic review of literature published between 2010 and 2024 in databases including PubMed, Scopus, Web of Science, and Google Scholar. Keywords such as “Endometriosis,” “Stem Cell Therapy,” “Mesenchymal Stem Cells,” and “Cell-based Therapy”

were used. Of the 187 articles identified, 42 studies meeting inclusion criteria and directly evaluating the use of MSCs in endometriosis models (preclinical or clinical) were selected for in-depth analysis.

Results: The reviewed studies consistently demonstrate the therapeutic potential of MSCs in treating endometriosis. MSCs derived from adipose tissue, bone marrow, umbilical cord, and amniotic fluid were shown to reduce lesion size by up to 70% in animal models. They also modulated immune responses by increasing Tregs and reducing Th17 cells and M1 macrophage activity. MSCs inhibited angiogenesis through the downregulation of VEGF, PDGF, and MMP-9, and reduced fibrosis and adhesions by suppressing fibrogenic pathways (TGF- β /Smad, Wnt/ β -catenin). Additionally, they promoted tissue regeneration in the peritoneum and ovaries via growth factors like HGF and IGF-1. Early clinical trials reported reduced pain symptoms and improved fertility, with no major adverse events. The integration of MSCs with biomaterials such as nanoparticles and hydrogels further enhanced targeted delivery and therapeutic outcomes.

Conclusion: Stem cell therapy represents a novel, multifaceted approach to endometriosis by targeting its core pathological mechanisms: inflammation, immune dysregulation, angiogenesis, and fibrosis.

Keywords: Reproductive Disease, Endometriosis, Stem Cell Therapy

Os-12: Modulation of Arterial Blood Gas Following Nebulization of Extracellular Vesicles in an Experimental Model of Acute Respiratory Distress Syndrome in Sheep

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Objective: Recent research in preclinical settings suggests that the use of extracellular vesicles (EVs) as a novel therapeutic strategy can lead to beneficial outcomes and has raised new hopes for recovery in patients, as these vesicles can induce anti-inflammatory, anti-apoptotic, and tissue repair effects. This study aimed to investigate the effect of extracellular vesicles derived from adipose tissue mesenchymal stem cells (ADM-SCs-EVs) on arterial blood gas in an experimental model of acute respiratory distress syndrome (ARDS) in sheep.

Materials and Methods: Six male sheep were randomly divided into two groups: treatment (recipient of ADMSCs-EVs) and control (recipient of ADMSCs culture medium). EVs were isolated from ADMSCs and confirmed. ARDS was induced in both groups via intratracheal administration of lipopolysaccharide from *E. coli* 055:B5. After one day and confirmation of ARDS, EVs were nebulized into the lungs of the treatment

group, while the control group received the culture medium. Arterial blood samples were taken before ARDS induction and at 12, 24, 48, 72, and 168 hours after nebulization. Oxygen partial pressure (PO₂), carbon dioxide partial pressure (PCO₂), and oxygen saturation (SatO₂) were measured using a blood gas analyzer.

Results: After ARDS induction, levels of PO₂ and SatO₂ decreased significantly, while PCO₂ increased significantly. However, following ADMSCs-EVs nebulization, arterial blood gas analysis showed a significant increase in PO₂ and SatO₂ and a significant decrease in PCO₂ in the treatment group compared to the control group. In contrast, the control group, which did not receive any specific treatment, continued to show a decrease in PO₂ and SatO₂ and an increase in PCO₂ until the end of the study.

Conclusion: Nebulization of ADMSCs-EVs in an experimental model of ARDS in sheep showed promising results in modulating arterial blood gas levels. Based on these findings, EVs could be considered a potential treatment, although further studies are recommended.

Keywords: Extracellular Vesicles, Nebulization, Arterial Blood Gas, Acute Respiratory Distress Syndrome, Sheep

Os-13: Nano-Chemo-Immunotherapy for Glioblastoma: Cyclophosphamide-Loaded Dual-Targeted Chitosan Nanoparticles for Immune Activation in Orthotopic Rat Models

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Objective: Glioblastoma (GBM) is characterized by an immunosuppressive tumor microenvironment (TME) that limits the efficacy of current therapies. Conventional chemotherapy alone fails to elicit a durable immune response. This study investigates a novel nano-chemo-immunotherapeutic strategy using cyclophosphamide (CP)-loaded chitosan nanoparticles modified with D8 and RI-VAP peptides to induce immunogenic cell death (ICD), promote immune activation, and reprogram the GBM TME from immunologically “cold” to “hot.”

Materials and Methods: CP was encapsulated in chitosan nanoparticles (NPs) functionalized with D8 (for blood-brain barrier crossing) and RI-VAP (for glioma targeting). The nanoparticles were characterized using dynamic light scattering (DLS), scanning electron microscopy (SEM), and zeta potential. ICD induction was evaluated by HMGB1 release. Immune activation was assessed through dendritic cell (DC) maturation markers (CD86+, CD11c+) and T-cell infiltration (CD4+, CD8+) into the tumor site.

Results: CP-loaded dual-targeted NPs effectively induced ICD, with significant HMGB1 release. Enhanced DC maturation and increased infiltration of CD8+ and CD4+ T cells were observed in tumor tissue, indicating robust immune activation. Preliminary survival data suggest therapeutic benefit in orthotopic C6 glioma rat models.

Conclusion: This nano-chemo-immunotherapy approach shows promising potential for glioblastoma treatment by combining targeted drug delivery with immune stimulation. Preliminary in vivo findings suggest that the dual-targeted system not only penetrates the blood-brain barrier but also transforms the immunologically “cold” glioma tumor microenvironment into a “hot” one, thereby enhancing antitumor immunity.

Keywords: Glioblastoma, Chitosan Nanoparticles, Blood-Brain Barrier, Nano-Chemo-Immunotherapy, Immunosuppressive Tumor Microenvironment

Os-14: Pan-Cytokeratin Expression of Mesenchymal Stem Cells Cultured on Chitosan/Polyvinyl Alcohol Hydrogel Containing Caviar Extract

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Objective: The development of wound dressings with optimal properties is crucial for accelerating the wound healing process. The aim of this study was to investigate the expression of the Pan-cytokeratin protein in stem cells cultured on a hydrogel-based wound dressing synthesized from chitosan (CS), polyvinyl alcohol (PVA), and caviar extract (Ce).

Materials and Methods: The CS/PVA/Ce hydrogel was synthesized using a freeze-drying method, and its structural properties were evaluated by scanning electron microscopy (SEM). The biocompatibility and metabolic activity of adipose tissue-derived stem cells (ADSCs) seeded on the optimized hydrogels were assessed after 24 hours using an MTT assay. The expression of Pan-cytokeratin protein was evaluated by immunohistochemistry (ICC) in the cells treated with the hydrogel.

Results: The SEM images revealed that the hydrogel has a dense, porous, and coherent structure. The MTT results indicated that the cells maintained proper morphology and exhibited increased metabolic activity when treated with the designed hydrogel. The ICC images showed that the prepared hydrogel enhanced the expression of Pan-cytokeratin protein.

Conclusion: The CS/PVA hydrogel containing caviar extract demonstrated great potential for inducing Pan-cytokeratin protein expression, making it a promising material for wound healing applications.

Keywords: Adipose-Derived Mesenchymal Stem Cells, Pan-Cytokeratin, Hydrogel, Caviar Extract, Wound Healing

Os-15: Obstetrical Waste Extracellular Matrix-Based Materials Implanted in Sponge Scaffold Form Versus Powder Form: Which One Has a Promising Application for Tissue Engineering?

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Objective: The application of materials derived from birth delivery, such as amniotic membrane, umbilical cord, and placenta, has gained attention in tissue engineering due to their cost-effectiveness and other beneficial properties. This study investigates the potential use of these materials in tissue engineering, specifically their extracellular matrix (ECM) components.

Materials and Methods: Amniotic membrane (AM) and umbilical cord (UC) were decellularized to extract their corresponding ECM, which was processed into two forms: sponge (S) and powder (P). These materials were then implanted in manually created full-thickness wounds. Histopathological evaluations were performed at the implantation site on days 10 and 20 post-implantation.

Results: Histopathological evaluations of lesions on day 10 post-incision revealed similar characteristics in all treatment groups, with the presence of immature granulation tissue and infiltration of inflammatory cells. However, re-epithelialization did not occur in these treatments. Notably, the sponge form of the UC treatment group showed a significantly higher deposition of collagen fibers compared to the others. On day 20, the micrographs of the sponge forms of AM and UC showed similar results in terms of collagen density and re-epithelialization. Inflammatory cells were significantly reduced in the wounds treated with the sponge forms of UC, while the corresponding evaluation of the powder forms of both treatment groups (AM and UC) revealed a significantly higher inflammatory response. Furthermore, re-epithelialization remained incomplete in the powder form treatments.

Conclusion: The sponge form of UC demonstrated the most promising results, indicating its potential as a material derived from birth delivery for use in tissue engineering and regenerative medicine.

Keywords: Tissue engineering, Decellularization, Amniotic membrane, Umbilical cord, Extracellular matrix

Poster Presentations

Ps-1: Chitosan-Selenium Nanoparticles Containing Quercetin: Synthesis, Characterization, and Neuroprotective Effects

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Objective: Cisplatin is a widely used chemotherapy drug that significantly improves survival rates in patients with various cancers, including lymphomas, breast, testicular, ovarian, head and neck, lung, cervical, bladder, and sarcomas. Despite its effectiveness, the clinical application of cisplatin is often limited by its severe side effects, particularly neurotoxicity. Quercetin, a flavonoid antioxidant found in many fruits and vegetables, has demonstrated the ability to reduce cisplatin-induced neurotoxicity in various experimental models, yet its clinical use is restricted by poor solubility, rapid metabolism, and low bioavailability. To overcome these challenges, we developed chitosan-selenium nanoparticles containing quercetin (Q-Cs@Se NPs), which combine selenium's antioxidant properties and chitosan's positive charge to enhance quercetin delivery.

Materials and Methods: The nanoparticles were synthesized in three steps to create a layer-by-layer structure. The as-prepared nanoparticles were characterized using UV-Vis spectroscopy, Fourier transform infrared spectroscopy (FTIR), dynamic light scattering (DLS), zeta potential analysis, energy-dispersive X-ray spectroscopy (EDX), and transmission electron microscopy (TEM). Finally, the protective effects of the nanoparticles against cisplatin-induced neurotoxicity in PC12 cells, a neuronal cell model, were evaluated using the MTT assay and flow cytometry analysis.

Results: In this study, Q-Cs@Se nanoparticles were synthesized with an average size of 110 nm and a zeta potential of +11.5 mV. According to the MTT assay, a 24-h pretreatment with Q-Cs@Se nanoparticles (1.25 µg/mL) increased the viability of PC12 cells exposed to cisplatin at its IC₅₀ concentration from 50% to nearly 80%. Furthermore, Q-Cs@Se nanoparticles significantly reduced cisplatin-induced apoptosis and necrosis in PC12 cells.

Conclusion: The findings indicate that Q-Cs@Se nanoparticles have potential as neuroprotective adjuvants to improve the safety profile of cisplatin treatment; however, further research is needed to confirm their efficacy and safety.

Keywords: Selenium nanoparticle, Quercetin, Cisplatin, Neurotoxicity

Ps-2: Preparation, Optimization, and Characterization of Chondroitin Sulfate-Coated Cationic Nanomicelles for Sorafenib Delivery

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Objective: Sorafenib is the established first-line treatment for patients with advanced hepatocellular carcinoma. However, its undesirable systemic effects and altered pharmacokinetics due to low solubility affect its clinical application. Nanomicelles are promising drug carriers in cancer therapy because they are small, affordable, easy to prepare, and can efficiently encapsulate hydrophobic drugs. In this study, considering the higher toxicity and permeability of positively charged nanoparticles in cancer cells, cationic micelles (Tween80/CTAB) were developed for loading sorafenib. To improve nanoparticle stability and cancer cell targeting, the micelles were coated with chondroitin sulfate, which binds to the CD44 receptor overexpressed in tumors.

Materials and Methods: Cationic nanomicelles were simply synthesized using a solvent evaporation method with CTAB and Tween80. The synthesis process was optimized using central composite design (CCD) to achieve nanomicelles with the smallest possible size and highest encapsulation efficiency (EE). Three factors were considered for optimization: sorafenib concentration, CTAB/Tween80 ratio, and sonication time. The optimal nanomicelles were then coated with chondroitin sulfate. The resulting nanomicelles were characterized by dynamic light scattering and zeta potential analysis.

Results: This study used a reduced cubic model obtained by backward elimination regression to analyze the relationship between the studied factors and the responses. The optimum conditions for nanomicelle synthesis were determined as follows: sonication time of 5 minutes, CTAB/Tween80 ratio of 0.4, and sorafenib concentration of 100 µg/mL. Due to the equation obtained using CCD, the predicted size and encapsulation efficiency under optimal conditions were 47 nm and 75%, respectively. When the optimal nanomicelles were coated with chondroitin sulfate, the zeta potential changed from +23.7 to +2.5 mV, indicating the attachment of negatively charged chondroitin.

Conclusion: The optimized chondroitin sulfate-coated cationic nanomicelles showed potential as targeted carriers for sorafenib delivery. Further In vitro and In vivo studies are necessary to confirm their therapeutic efficacy and safety.

Keywords: Sorafenib, Nanomicelle, Chondroitin Sulfate, Cancer

Ps-3: Comparative Evaluation of Intratesticular Injection of Mesenchymal Stem Cells and MSC-Derived Exosomes in Treating Busulfan-Induced Azoospermia in Rats

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Objective: Mesenchymal stem cells (MSCs) and their derived exosomes have shown promising regenerative effects in treat-

ing male infertility. In this study, we focus on comparing the therapeutic efficacy of MSC transplantation versus MSC-derived exosomes in restoring spermatogenesis in a rat model of busulfan-induced azoospermia.

Materials and Methods: Azoospermia was induced in adult male Wistar rats (n=40) via a single intratesticular injection of busulfan (5 mg/kg). After 60 days, azoospermia was confirmed via sperm analysis. Rats were randomized into five groups (n=8): healthy control, azoospermic control, MSC-treated, exosome-treated, and PBS-treated. MSCs were isolated from rat bone marrow, characterized, and expanded. Exosomes were collected from MSC-conditioned medium. Treatments included intratesticular injection of either 1×10^6 MSCs or 100 μ g exosomes. After 60 days, sperm parameters, DNA fragmentation (TUNEL assay), hormone levels (FSH, LH, testosterone), and testicular histopathology were assessed.

Results: Both MSC and exosome treatments significantly improved sperm count, motility, and morphology compared to the azoospermic control group ($p < 0.05$). DNA fragmentation levels decreased notably in both treated groups. Serum hormone levels (FSH, LH, and testosterone) were restored closer to normal values following treatment. Histopathological analysis revealed improved seminiferous tubule structure and the presence of spermatozoa in the lumen in both MSC and exosome groups. Notably, the MSC-treated group exhibited slightly greater improvements across all parameters compared to the exosome-treated group.

Conclusion: Both MSC transplantation and MSC-derived exosomes effectively improve spermatogenesis in busulfan-induced azoospermic rats. However, MSC transplantation demonstrated a slightly greater regenerative effect, possibly due to the cells' ability to home and differentiate within the testicular tissue. Meanwhile, exosomes represent a promising, safer, and cell-free therapeutic alternative.

Keywords: Mesenchymal Stem Cells, MSC-Derived Exosomes, Azoospermia, Male Infertility

Ps-4: Development and Validation of a Serum-Based mRNA-miRNA Biomarker Panel for Non-Invasive Diagnosis of Multiple Sclerosis

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Objective: Multiple sclerosis (MS) is a chronic autoimmune disorder of the central nervous system, where timely diagnosis remains challenging due to reliance on invasive procedures like spinal tap or costly MRI scans. Non-invasive biomarkers are urgently needed to streamline diagnosis, reduce patient burden, and accelerate therapeutic interventions.

Materials and Methods: We designed a serum-based biomarker panel by integrating the analysis results of mRNA and miRNA profiles from MS patients and healthy controls. Gene Expression Omnibus (GEO) datasets GSE21942 (mRNA, 14 MS/15 controls) and GSE43591 (mRNA, 10 MS/10 controls) and miRNA data from GSE17846 (20 MS/21 controls) were analyzed. Differentially expressed genes (DEGs) and miRNAs

(DEMs) were identified using LIMMA in R ($|\log FC| > 1$, $*p < 0.05$), visualized via volcano/heat-maps. Protein-protein interaction (PPI) networks of DEGs were constructed in Cytoscape, while TargetScan predicted miRNA-mRNA interactions.

Results: Intersecting DEGs and DEM targets revealed hub genes, including LYZ, CXCL8, FPR2, and MMP9, alongside miRNAs like hsa-mir-199a-5p and hsa-mir-532-3p. Functional enrichment (GO/KEGG) highlighted immune-regulation pathways. ROC analysis demonstrated strong diagnostic accuracy ($AUC > 0.85$) for the combined panel.

Conclusion: Our study findings highlight some key protein-coding genes and miRNAs that are involved in the occurrence and evolution of MS. The panel may support precision medicine by offering a rapid, cost-effective diagnostic tool, potentially improving early intervention and personalized patient management.

Keywords: Multiple sclerosis, non-invasive diagnosis, biomarkers, mRNA-miRNA

Ps-5: Mesenchymal Stem Cells (MSCs) in Infertility and Reproductive Tissue Regeneration

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Objective: The reason behind millions of worldwide cases of infertility rests with terminal damage to reproductive tissues. The current reproductive assistance treatments known as assisted reproductive technologies (ART) present limited help for patients. Research has now focused on Mesenchymal Stem Cells (MSCs) because these cells demonstrate three essential characteristics: regenerative, paracrine, and immunomodulatory properties. The review investigates existing research evidence related to MSC usage for treating infertility along with reproductive tissue restoration by identifying therapeutic obstacles as well as fundamental cellular processes.

Materials and Methods: Researches covering this subject spanned from 2010 to 2025 through PubMed and Scopus and Web of Science database searches. Both preclinical studies and clinical trials involving MSCs for treatment of ovarian failure alongside endometrial damage and male infertility were included in the review. The investigators dedicated their research to explain regenerative mechanisms through exosomes as well as paracrine signaling and immunomodulatory processes.

Results: Studies consistently demonstrate that MSCs promote angiogenesis, inhibit apoptosis, and modulate fibrotic pathways primarily through the TGF- β /Smad and PI3K/Akt signaling cascades. MSC-derived exosomes, rich in regenerative microRNAs (e.g., miR-21, miR-126), contribute substantially to tissue repair. Despite promising results, heterogeneity in MSC sources, dosing regimens, and delivery methods presents major limitations. Additionally, long-term safety and efficacy data remain scarce.

Conclusion: MSCs provide a new regulatory method for infertility treatment which uses restorative processes that extend past cell substitution. Future research needs to establish standardized therapeutic procedures along with exosome intervention analysis in order to achieve translation success. Strategic advances in these areas could transform MSC-based therapies from experimental models into mainstream clinical practice.

Keywords: Mesenchymal Stem Cells (MSCs), Reproductive Tis-

sue Regeneration, Infertility treatment, Paracrine Signaling Pathways, Cellular Differentiation

Ps-6: Fabrication and Evaluation of Bioactive Core-Shell Nanofibrous PCL/PAN Scaffolds for Bone Tissue Engineering Applications

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Objective: For more than two decades, many efforts have been made in the development of biomaterials and fabrication techniques to present a suitable substitute in the field of bone tissue engineering. A fine-tuned combination of scaffolds, biomolecules, and stem cells can be used in this field to maintain and restore the function of injured bone tissue and overcome the difficulties associated with its regeneration. To this aim, we represent a promising approach, consisting of poly(ϵ -caprolactone) (PCL)/ polyacrylonitrile (PAN) reinforced with hydroxyapatite (HA) and silver (Ag) nanoparticles for efficient osteogenic differentiation of human adipose derived mesenchymal stem cells (ADMSCs).

Materials and Methods: Electrospun PCL/PAN (core-shell) scaffolds include HA and Ag nano particles were produced in 2D sheets with coaxial electrospinning technique. The fibers diameter, fibers alignment and mechanical properties have been evaluated, and the impact of HA and Ag incorporation on cell viability and behavior and also osteogenic differentiation capacity of ADMSCs were assessed.

Results: Coaxial PCL-PAN/HA/Ag nano-fibrous scaffolds exhibited suitable structural and mechanical properties and higher bioactivity and anti-bacterial activity compared to PCL/PAN scaffolds due to the surface exposure of the HA and Ag nanoparticles. Coaxial scaffolds with and without HA supported ADMSCs proliferation and exhibited more expression of osteogenic related genes, alkaline phosphatase activity and calcium content with significant difference between the other scaffolds types.

Conclusion: Our findings demonstrated the osteoinductive potential of coaxial PCL/PAN nano-fibrous scaffolds, and suggest that its combination with HA/Ag nanoparticles might be a great promising option in bone tissue engineering applications.

Keywords: coaxial electrospun scaffolds, nanoparticles, Adipose derived mesenchymal stem cells, , osteogenic differentiation

Ps-7: Comparative Analysis of Linear and Stem-Loop Probes for Detection of miR-21-5p in Cancer Cells Using an AuNP-Based Biosensor

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Objective: MicroRNA-21-5p (miR-21), a key cancer biomark-

er, requires sensitive detection methods. Here, we evaluated linear vs. stem-loop ssDNA probes in an unmodified AuNP colorimetric biosensor for miR-21 detection in cancer cells.

Materials and Methods: Gold nanoparticles (AuNPs, ~20 nm) were synthesized via citrate reduction and functionalized with NH₂-modified ssDNA probes targeting miR-21. Upon NaCl addition, unprotected AuNPs aggregate, producing a red-to-blue color change observable by eye and quantifiable by UV-vis spectroscopy. Aggregation dynamics and size distribution changes were characterized by dynamic light scattering (DLS) and transmission electron microscopy (TEM).

Results: Both linear and stem-loop probes enabled sensitive miR-21 detection; however, the stem-loop probe exhibited superior specificity in discriminating the target miRNA from closely related sequences. The UV-vis spectrophotometry confirmed a distinct red-to-blue shift, correlating with increasing miR-21 concentrations. Stem-loop probes yielded a higher signal-to-noise ratio. The biosensor achieved detection in the nanomolar range and successfully identified miR-21 in cancer cell lysates, highlighting its potential for clinical applications.

Conclusion: This work provides valuable insights into probe design for miRNA detection, emphasizing the advantages of stem-loop structures in enhancing specificity for point-of-care diagnostic platforms.

Keywords: miRNA, Cancer detection, Gold nanoparticles, Colorimetry biosensor

Ps-8: Autophagy Modulation Can control the Angiogenesis Properties of Human Endothelial Progenitor Cells in A 3D Culture System

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Objective: Endothelial progenitor cells (EPCs) exhibit promising regenerative potential in ischemic tissues and various pathologies. The effect of autophagy response in the function of EPCs has not been exactly addressed. This study aimed to evaluate the modulation of autophagy in EPCs cultured on alginate-gelatin hydrogel over 5 days.

Materials and Methods: Human EPCs were isolated from expanded bone marrow aspirates and characterized using different assays. Cells from passage 3, were overlaid on 1% alginate/gelatin hydrogel cross-linked using 0.2 mM CaCl₂ and incubated with metformin and/or hydroxychloroquine for 5 days. The angiogenesis properties of EPCs were monitored in terms of migration, survival, and autophagy using Transwell insert assay, MTT, and PCR array analysis.

Results: Data indicated typical spindle-shaped EPCs with typical colonies having numerous outgrowth cells. The isolated cells express CD133, CD34, VGFR-2, and Tie-2 as typical biomarkers for the characterization of EPCs. The ability of EPCs to uptake Dil-AC-LDL indicated their suitable functionality. Data confirmed the lack of toxicity in cultured EPCs on the alginate-gelatin surface in the presence or absence of autophagy biomarkers. PCR array analysis revealed the autophagy-related genes in metformin-treated EPCs compared to the control and hydroxychloroquine groups. The migration of EPCs was induced in the presence of metformin related to other experimental groups. It seems that both autophagy activation or inhibition by metformin and hydroxychloroquine can accelerate the maturation of EPCs to mature endothelial cells indicated by vWF and VE-cadherin.

Conclusion: Autophagy modulation can influence the angiogenesis properties of EPCs in vitro via the increase of maturation into endothelial cells.

Keywords: Endothelial progenitor cells, Angiogenesis, Autophagy, Alginate/Gelatin hydrogel

Ps-9: Expression and Functional Assay of Recombinant EcoRI Restriction Endonuclease in *E. coli*

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Objective: *Escherichia coli* strain RY13 Restriction Endonuclease I (EcoRI) plays a critical role in genetic engineering, enabling precise DNA manipulation for cloning and epigenetic studies due to their sequence-specific DNA cleavage ability. However, due to high cost and import challenges of commercial EcoRI, in-house production is needed to provide cost-effective access to key molecular tools, supporting in-house research and biotechnological progress.

Materials and Methods: The EcoRI gene was cloned into the pET28a expression vector and transformed into *E. coli* BL21(DE3) and Rosetta-gami B(DE3) pLysS strains. Protein expression was induced by using IPTG and purified with Ni-affinity chromatography. The recombinant enzyme's activity and stability were evaluated through standard assays and compared with a commercial EcoRI sample.

Results: BL21(DE3) produced higher recombinant protein yields compared to Rosetta-gami B(DE3) pLysS (approximately 200 µg of purified enzyme, equivalent to 20,000 activity units per one liter of culture). Based on material and reagent costs, the in-house production cost was estimated to result in a 30–40% reduction. In addition, the recombinant EcoRI showed high cleavage activity, comparable to the commercial enzyme. The enzyme maintained its functional activity in standard digestion assays and demonstrated reasonable thermal and chemical stability.

Conclusion: This study demonstrates the feasibility of producing recombinant EcoRI in *E. coli* BL21(DE3) with competitive efficiency with appropriate activity comparable to commercial enzyme. This approach supports local biotechnology by reducing

import dependency and providing affordable access to essential molecular tools for research and applied purposes.

Keywords: EcoRI, Recombinant protein, *E. coli*, Restriction enzyme

Ps-10: Apoptotic Effects of Linarin and Its Derivatives on MDA-MB-231 Breast Cancer Cells: A Molecular and Cellular Investigation

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Objective: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer with limited therapeutic options due to the absence of hormone receptors and HER-2 expression. Linarin, linarygenin, and propargyl linarin—flavonoids extracted from the hydroalcoholic extract of **Salvia** species—exhibit antioxidant, anti-inflammatory, and pro-apoptotic properties. This study investigates the apoptotic effects of these compounds on MDA-MB-231 cells, focusing on key molecular mechanisms and potential therapeutic pathways.

Materials and Methods: MDA-MB-231 cells were cultured in DMEM supplemented with 10% FBS and antibiotics. Cytotoxicity of linarin, linarygenin, and propargyl linarin was assessed using the MTT assay, and IC50 values were determined. Apoptosis was evaluated through Annexin V/PI staining followed by flow cytometry, while cell cycle arrest was analyzed at the IC50 concentration using PI staining. Western blotting was performed to assess the inhibitory effect of these compounds on STAT3 phosphorylation and the expression of apoptotic markers such as Bax, Bcl-2, and Caspase-3.

Results: Linarin, Pectolinarygenin, and propargylated pectolinarygenin exhibited IC50 values of 500 µg/ml, 22 µg/ml, and 105 µg/ml, respectively. Treatment with these compounds significantly reduced cell viability in a dose- and time-dependent manner. Flow cytometry revealed increased early and late apoptotic cells post-treatment, particularly with two derivatives. Western blot analysis confirmed upregulation of pro-apoptotic proteins (Bax, Caspase-3) and downregulation of anti-apoptotic proteins (Bcl-2). Additionally, all compounds inhibited STAT3 phosphorylation, highlighting their role in disrupting cell survival pathways.

Conclusion: This study demonstrates the potent apoptotic effects of linarin and its derivatives on MDA-MB-231 cells through modulation of intrinsic apoptotic pathways and STAT3 inhibition. The findings suggest these compounds, especially pectolinarygenin and propargylated pectolinarygenin, as promising candidates for TNBC therapy, warranting further preclinical studies.

Keywords: Linarin, STAT3 inhibition, MDA-MB-231, triple-negative breast cancer, apoptosis

Ps-11: Creation Of a Recombinant Construct Containing The PDX1 Gene Using The CRISPR/Cas9 System

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Objective: Homeodomain transcription factor 1 (PDX-1) is crucial for the survival of pancreatic β cells. It plays a key role in normal pancreatic development and growth by directing the maturation and differentiation of pancreatic progenitor cells. Therefore, PDX-1 is necessary for proper pancreatic development and β cell function. This study aims to create a mutation in the PDX-1 gene of chicken by designing a complementary gRNA to a part of the PDX-1 gene, which is cloned into a lentiviral vector containing the CRISPR/Cas-9 construct

Materials and Methods: To induce deletion and modifications in the PDX-1 gene of chicken, a single guide RNA (sgRNA) sequence was designed using the CRISPR Design Tool online software. It was cloned into the LentiCRISPRv2GFP lentiviral vector using restriction enzymes and ligation reactions and transformed into the host cells *Escherichia coli* Top10 through heat shock. To ultimately confirm the successful cloning of the sgPDX-1 gene, the bands obtained from the colony PCR method were sequenced.

Results: The 20 nucleotide sgRNA fragment, complementary to exon 1 of the PDX-1 gene, was cloned into the LentiCRISPRv2GFP vector. Using specific primers, a 267bp fragment was amplified from the transformed colonies. The presence of this fragment in the vector was confirmed through sequencing. Additionally, enzymatic digestion with the restriction enzymes Bmsb1 and EcoRV revealed a 2000bp fragment containing the cloned piece, which was observed in an agarose gel.

Conclusion: This study represents the first report of the creation of a recombinant construct containing a recombinant fragment of the PDX-1 gene along with the CRISPR/Cas9 array in lentiviral vectors. The generated genetic construct holds significant potential for gene function studies and gene therapy applications. This system is also one of the most suitable methods for developmental studies in chicken embryos

Keywords: PDX-1 gene, CRISPR/Cas-9 system, Chicken embryo, sgRNA

Ps-12: Evaluation of the Function of the PDX1 Gene-Carrying Lentiviral Construct in Chicken Embryonic and Human Cells

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Objective: The chicken embryo has a long history as a model in the field of developmental biology, studying disease progression, gene function during tissue and organ development, and the differentiation and regenerative capabilities of human cells in the natural body environment. Therefore, this study aims to generate lentiviral vectors carrying the PDX1 gene using the CRISPR/Cas9 system in HEK293T-LentiX cells. In the future, we plan to provide a practical foundation for research by directly transferring these recombinant viral vectors into embryos and chicken cells

Materials and Methods: Lentiviral particles were produced from HEK293T-LentiX cells. GFP expression was observed using a fluorescence microscope to determine viral titer, and viral titer was measured using flow cytometry. To assess virus functionality, lentiviral particles were transferred into chicken and human cells, and the presence of the recombinant construct was confirmed using a fluorescence microscope.

Results: High-titer lentiviral particles were successfully produced. The HEK293T cells were infected with virus particles, and after 24 hours, more than 90% of the HEK293T cells showed GFP expression. This viral titer was evaluated and confirmed in HT1080 cells using flow cytometry. The presence of the virus in Fibroblast and Pancreatic chicken cells was observed.

Conclusion: The lentiviral vectors carrying the PDX1 gene, produced using the CRISPR/Cas9 system, demonstrated high transfer efficiency both in vitro and in vivo. Therefore, these vectors can be used to introduce desired genes into primary gamete cells under the control of specific tissue promoters, which will produce genetically modified birds with beneficial biotechnological traits.

Keywords: Chicken embryo, lentiviral vectors, Chicken fibroblast cell, PDX1 gene

Ps-13: A Teratocarcinoma Cell-based Embryonic Model for Assessing the Teratogenic Effects of Chemical Compounds

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Objective: Teratogens are compounds that cause birth defects in developing fetuses. The recognition of thalidomide's harmful effects on limb development in the 1960s heightened awareness of teratogenicity. Methods to identify teratogens include drug testing on pregnant animals, human epidemiological studies, and pluripotent stem cell research. While animal testing offers controlled experimentation, it faces challenges such as high costs, interspecies variations, and ethical concerns. Non-animal alternatives like in vitro assays using pluripotent stem cells have gained traction. This study focuses on embryonic carcinoma cells, which can undergo axial elongation morphogenesis in vitro, aiding teratogen identification.

Materials and Methods: A thorough search of the PubMed and Web of Science databases has been conducted up to April 2025, without time restrictions. This search integrates terms from MeSH databases related to Embryonic Carcinoma Stem Cells, differentiation, and embryoid body.

Results: Two teratocarcinoma cell lines resembling early mouse embryonic cells have been identified, capable of axial elongation morphogenesis in vitro through aggregation. The P19 cell line, from standard embryonic teratocarcinoma, shows characteristics similar to the epiblast and differentiates into various cell types, demonstrating gene expression patterns typical of posterior mesoderm. The F9 cell line, derived from a testicular teratoma, can also differentiate into all three germ layers. Both cell lines exhibit traits of early embryonic cells and can respond to agents to induce further differentiation.

Conclusion: Many teratocarcinoma cells exist, but only a few can form embryoid bodies to generate germ layers. P19 cells are used for teratogenicity testing; F9 cells may simulate embryos, highlighting the need for human-derived cell studies.

Keywords: Embryonic Carcinoma Stem Cells, Differentiation,

Embryoid body, Teratogenesis

Ps-14: Induction of Neuronal Differentiation in Human Retinoblastoma Cells Using Retinoic Acid and Isotretinoin

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Objective: Retinoblastoma is a common childhood eye cancer that can invade the entire eye and surrounding tissues. The main treatment is chemotherapy, but it has side effects, especially in children, and issues like drug resistance and recurrence often arise. Differentiation therapy offers an adjunct approach by transforming cancer cells into normal-like cells, neutralizing their cancerous properties. Retinoic acid (RA) and isotretinoin are promising agents for this therapy, as RA influences around 500 genes crucial for eye and embryonic development.

Materials and Methods: In this experimental study, the human Y79 retinoblastoma cell line at passage 20 was treated with five concentrations of RA and isotretinoin in both suspension and adherent culture conditions. The aim was to evaluate their effects on cellular differentiation, including morphological changes and immunocytochemical marker expression.

Results: Cells were exposed to 5, 10, 20, 30, and 50 μ M doses of RA and isotretinoin under both culture conditions. In suspension cultures, cell numbers declined significantly starting from day 3, with complete cell loss by day 9. In adherent cultures, morphological changes emerged from day 3 at 20 μ M, and at 30 and 50 μ M, these changes appeared earlier, although cell viability decreased considerably. The 20 μ M concentration of both agents was selected as optimal for further differentiation studies. Morphological alterations intensified until day 18, reaching a peak, followed by extensive cell death by day 21. Immunofluorescence studies showed no expression of NEUN or VGLUT1 in untreated cells; in contrast, treated cells exhibited positive expression of both markers, indicating differentiation.

Conclusion: Retinoblastoma cells, normally maintained in suspension, require attachment to pre-coated plates to differentiate. The expression of NEUN suggests neuronal maturation, while VGLUT1 expression in bipolar and photoreceptor cells indicates differentiation toward these specialized cell types.

Keywords: Retinoblastoma, Differentiation therapy, Retinoic acid, Isotretinoin

Ps-15: The Effect of Papaver Somniferum Extract and Tamoxifen on the Expression of Autophagy Pathway Genes, CDK4, MiR-146a And MiR-22 In Du145 Prostate Cancer Cell Line

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Objective: Prostate cancer is prevalent malignancy in men, and conventional therapies often exert dramatic side effects. Papa-

ver somniferum extract exhibit promising anticancer properties with a potential for reducing adverse effects of cancer. This study aimed to evaluate the antiproliferative and cytotoxic effects of Papaver somniferum extract on Du145 prostate cancer cells and compare its efficacy with tamoxifen.

Materials and Methods: IC50 of tamoxifen and Papaver somniferum extracts was determined on Du145 cells using the MTT(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide assay. Three groups were designed for this study: 1) control group (Du145 prostate cancer cell line was harvested in the flask without treatment), 2) the cell lines treated with IC50 of tamoxifen ($37.53 \pm 1.9 \mu\text{g/mL}$), and 3) the cell lines treated with IC50 of Papaver somniferum extract ($77.37 \pm 2.7 \mu\text{g/mL}$) for 72 hours. Real-time PCR was used to assess changes in expression of CDK4 (cell cycle controlling and regulation), miR-146a (suppressor of BRCA1 gene), and miR-22 (suppressor of P53). Data were analyzed using SPSS software and one-way ANOVA and expressed as means $\pm$ SD, $p < 0.05$ was considered significantly

Results: After 72 hours, The IC50 values for tamoxifen and P.somniferum extract were $37.53 \pm 1.9 \mu\text{g/mL}$ and $77.37 \pm 2.7 \mu\text{g/mL}$ respectively. Tamoxifen showed more toxicity than P somniferum extract, with maximum effect at 72 hours. Both treatments significantly ($p < 0.05$) reduced CDK4 expression and increased the expression of miR-22 and miR-146a compared to the control group, demonstrating their antiproliferative effects.

Conclusion: both Papaver somniferum extract and tamoxifen showed anti-proliferative effects on Du145 prostate cancer cells and influenced autophagy-related gene expression. Although tamoxifen was more potent, the extract also showed significant activity, indicating its potential in cancer therapy. Further research is needed to identify active compounds, evaluate in vivo efficacy, and assess safety before clinical use.

Keywords: Papaver somniferum extracts, tamoxifen, prostate cancer, CDK4, miR-146a

Ps-16: Simultaneous Inhibition Of WNT/ β -catenin and TGF- β Signaling Pathways By IWP-2 And SB431542 In Order to Reduce Cancerous Potential of Hepatocellular Carcinoma Cell Line

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Objective: Hepatocellular carcinoma (HCC) is the most common primary liver cancer with a rising incidence in the world. It will become one of the top cancer-causing mortality cases in the world by the year 2030. Current treatment methods are faced many challenges for HCC patients due to high rates of recurrence, developing therapy-resistance, the associated side effects, and therefore emphasizing the need for new or revised treatment or drug therapies.

Materials and Methods: One method that has emerged recently is to alter pathways that exhibit intracellular signaling dysregulation that play a prominent role in cancer progression. The WNT/ β -catenin and TGF- β signaling pathways, in particular, are well known to be critical in managing the essentials of HCC which include promoting proliferation, apoptosis, cell migration and invasion. In this project, two selective small-molecule inhibitors will be used to block signaling through these pathways

in hepatocellular carcinoma cells to reduce their malignancy. SB431542 blocks the TGF- β pathway by blocking the type I receptor and silencing downstream SMAD activation. IWP-2, on the other hand, blocks the porcupine enzyme required for post-translational modification and secretion of WNT ligands and thereby inhibits both canonical and non-canonical WNT signaling. Both of these drugs have already been shown to inhibit oncogenic activity in different cancers including lung, breast, and gastric cancer.

Results: By simultaneously blocking both pathways, we anticipate eradicating cell proliferation, migration, and invasion—characteristics of the malignant phenotype of HCC. This is in accordance with the principles of differentiation therapy, which is not intended to kill cancer cells themselves but restore their original features toward less malignant status, differentiated cell.

Conclusion: Overall, this dual-inhibition strategy offers a new and less toxic therapeutic avenue for the treatment of liver cancer, and promises to open a new door to more specific, molecular-based clinical therapy.

Keywords: Hepatocellular carcinoma, TGF- β , WNT/ β -catenin, IWP-2, SB431542

Ps-17: Investigation of the Effects of Butyric Acid on bFGF-induced IL-1 β Expression in MCF-7 Cell Line

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Objective: Inflammatory breast cancer (IBC) is one of the most aggressive types of breast cancer, characterized by severe inflammation and rapid progression. Chronic inflammation plays a key role in the progression and metastasis of this cancer, as inflammatory cytokines such as IL-1 β can alter the tumor microenvironment and promote the growth and survival of cancer cells. Butyric acid is a short-chain fatty acid with regulatory effects on gene expression. It is particularly noted for its ability to modulate the expression of inflammatory genes induced by basic fibroblast growth factor (bFGF) in breast cancer cells, suggesting its potential as a therapeutic agent in controlling inflammation and tumor progression. The results demonstrated a significant effect of butyric acid on IL-1 β expression, indicating that various butyric acid concentrations affect the inflammatory response in MCF-7 cells. This study aimed to investigate the effect of butyric acid on the expression of IL-1 β induced by bFGF in the MCF-7 breast cancer cell line.

Materials and Methods: In this fundamental study, human breast cancer cells (MCF-7) were cultured and bFGF was added to induce an inflammatory response, and then treated with butyric acid (0 μ M - 1.25 μ M - 2.5 μ M - 5 μ M) for 48 hours to evaluate their effects on IL-1 β expression. After treatment with various butyric acid concentrations, the RNA was extracted, and cDNA was synthesized for qRT-PCR analysis of IL-1 β . Statistical analyses were conducted.

Results: This study demonstrated that Butyric acid reduced IL-1 β expression in MCF-7 cells in 2.5 and 5 μ M concentrations ($p=0.044$ and $p=0.0001$, respectively). These results indicate butyric acid's potential to modulate inflammatory responses in breast cancer cells.

Conclusion: In conclusion, butyric acid significantly reduced IL-1 β expression in MCF-7 breast cancer cells ($p<0.05$), supporting its potential as an anti-inflammatory agent in breast cancer models.

Keywords: MCF-7 Cell Line, Sodium Butyrate, Butyric Acid, IL-1 β

Ps-18: Differentiation of Neural Cells Using TGFB1 Protein Inhibition

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Objective: In the present study, 42, 568 genes were analyzed, among which 3, 209 genes showed significant differential expression. To identify the key genes involved in this condition, a protein-protein interaction (PPI) network was constructed using the STRING database and visualized in Cytoscape. Using the CentiScaPe plugin, 30 critical hub genes were identified within the network. Among these, Tgfb1 was selected due to its highest down regulation in the pathway of stem cell differentiation into neural cells, with the aim of identifying an effective drug compound to promote differentiation.

Materials and Methods: One of the irreversible damages in living organisms, due to the low proliferation rate of neural cells, is spinal cord injury. Among the available treatment methods, cell therapy is one of the most recent therapeutic approaches that may be effective in recovering from spinal cord injuries.

Results: Ultimately, the compound JZL-184, exhibited through docking analysis using Molegro Virtual Docker (MVD) software, demonstrated the strongest interaction score (-175.865) with Tgfb1. For the first time, this study reports JZL-184 as a potential accelerator of neural differentiation of stem cells.

Conclusion: These findings may represent a step forward in the development of novel cell therapy strategies.

Keywords: Cell therapy, Spinal cord injury, Interaction network, Hub gene, Stem cell differentiation

Ps-19: Association of Rs328 With 10-Year Cardiovascular Disease Event in Subjects with Central Obesity

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Objective: Cardiovascular disease (CVD) is the most prevalent non-communicable disease globally. CVD is associated with risk factors include low-density lipoprotein (LDL). Lipoprotein lipase gene aids in the hydrolysis of triglyceride-laden particles. In this study, we investigated the association of the rs328 variant with a 10-year CVD event in subjects with central obesity.

Materials and Methods: The current study is a retrospective cohort analysis of the Mashhad Stroke and Heart Atherosclerotic Disorder (MASHAD) project, which began in 2010 and ended in 2020. Participants with central obesity were assessed for CVD using the major adverse cardiovascular events (MACE) criteria, and death rates were verified using the Iranian Ministry of Health's death registry. The study used SPSS for data analysis, including t-tests, COX regression, Kaplan-Meier plots, log-rank tests, and chi-square tests.

Results: Among the population, 335 individuals with an average age of 52.06±9.09 years encountered to the study. After adjusting for hypertension, age, and sex, the genotype model showed non-significant increased risks for CG (HR=2, p=0.066) and GG (HR=3, p=0.294) alleles compared to CC. However, the haplotype (G), (HR=2, p=0.033) and dominant (CG+GG), (HR=2, p=0.044) models remained significant.

Conclusion: The results of the current investigation indicated that rs328 was correlated with CVD events occurring within a decade. The GG genotype more than doubled the 10-year CVD event risk vs to the CC genotype.

Keywords: cardiovascular disease, central obesity, rs328, hypertension

Ps-20: Stem Cells in Heart Valve Tissue Engineering: A Systematic Review of Recent Advances and Future Directions

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Objective: Background: Cardiovascular diseases are among the most common diseases globally. There are many types and classifications, and heart valve disorders are among the most common, especially in children. Current treatment usually involves prosthetic replacement, which has many side effects, including blood clotting risk and fixed size that cannot be personalized or grow. Today, tissue engineering has introduced new approaches to producing living biocompatible heart valves. **Objective:** In this systematic review, we discuss the role of stem cells in heart valve tissue engineering (HVTE) and compare different cell types, their differentiation potential, and their functional outcomes in recent studies.

Materials and Methods: Methods: Related articles from databases including PubMed, Scopus, and Web of Science were searched between Jan 2015 and Feb 2025 using the following **Keywords:** "heart valve", "tissue engineering", "stem cells", "mesenchymal stem cells", "iPSCs", and "endothelial progenitor cells". Afterward, articles were chosen based on their applicability, structure, and the role of stem cells in them.

Results: Result: Finally, thirty-two studies met our inclusion criteria. Mesenchymal stem cells (MSCs) have been tested in many projects due to their easy accessibility and immunomodulatory role. While induced pluripotent stem cells (iPSCs) exhibited strong differentiation ability, they raise concerns due to their potential tumorigenicity. Furthermore, endothelial progenitor cells (EPCs) showed promising results in creating endothelial layers. Altogether, different classes of stem cells showed a wide range of positive effects, but there is a shortage of long-term in vivo results

Conclusion: Future studies should evaluate long-term functionality and ensure safe clinical translation.

Keywords: Cardiac Valve Bioengineering, Tissue-Engineered

Heart Valves (TEHVs), Stem Cell-Based Valve Reconstruction, iPSCs

Ps-21: Optimization and Quality Control of Autologous Fibrin Glue Production and Chondrocyte Culture for Cartilage Regeneration

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Objective: Articular hyaline cartilage is highly susceptible to injury, yet it possesses limited intrinsic regenerative capacity. Existing cartilage repair techniques predominantly result in fibrocartilage formation, which lacks the biomechanical and functional properties of native hyaline cartilage. As a result, regenerative strategies targeting hyaline cartilage has garnered significant interest. Chondrocytes, owing to their innate ability to produce hyaline cartilage matrix, are promising candidates for cartilage tissue engineering. Additionally, fibrin glue functions as a temporary extracellular matrix, supporting cell delivery and tissue integration. This study aims to optimize the production of autologous fibrin glue and the culture of autologous chondrocytes for application in the treatment of knee cartilage defects.

Materials and Methods: Autologous chondrocytes were isolated from patient cartilage tissue and expanded in vitro. Following confirmation of cell viability and proliferative capacity, a series of quality control tests were performed to verify maintenance of cellular phenotype and functional properties. Simultaneously, fibrinogen and thrombin were extracted from autologous plasma to produce fibrin glue, which was then subjected to physicochemical and mechanical strength.

Results: The identity and functionality of cultured chondrocytes were validated via RT-qPCR analysis of cartilage-specific markers (e.g., COL2A1, ACAN), Alcian Blue staining for proteoglycan synthesis, and karyotype analysis to confirm genomic stability and absence of microbial contamination. The fibrin glue formulation was optimized and validated based on protein concentration, clotting time, and physicochemical parameters, demonstrating appropriateness for clinical application. The final product met all established standards for safety, efficacy, and biocompatibility.

Conclusion: The integrated approach of autologous chondrocyte cultivation combined with fibrin glue—conceptually similar to commercially available Matrix-induced Autologous Chondrocyte Implantation (MACI)—has shown an 80–90% success rate in clinical studies for hyaline cartilage regeneration. Given the significant clinical need, the lack of domestically production, and the strategic importance for localization, this study aims to develop an indigenous manufacturing process. Preclinical evaluations are ongoing to facilitate regulatory approval and support future commercialization efforts.

Keywords: Fibrin glue, chondrocytes, knee cartilage defects, MACI

Ps-22: Stem Cell Secretions Offer a Safer and More Effective Therapy for Liver Fibrosis

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Objective: Liver fibrosis, a common consequence of chronic liver injury, currently lacks effective pharmacological treatments. In recent years, Mesenchymal Stem Cells (MSCs), particularly those derived from Wharton's Jelly (WJ-MSCs), have shown therapeutic potential due to their regenerative and immunomodulatory properties. However, concerns about their engraftment efficiency and safety have driven interest in cell-free therapies such as Conditioned Medium (CM) and Exosomes (Exo), which contain bioactive molecules secreted by MSCs. This study aimed to compare the anti-fibrotic efficacy of CM, Exo, and WJ-MSCs in a carbon tetrachloride (CCl₄)-induced mouse model of hepatic fibrosis.

Materials and Methods: After fibrosis induction, BALB/c mice were treated intraperitoneally with CM (100 µg/mouse, five doses), Exo (100 µg/mouse, five doses), or WJ-MSCs (1×10⁶ cells/mouse, two doses). The treatment effects were assessed by serum biochemical markers, histopathological staining, gene expression analysis, and immunohistochemistry.

Results: Our findings demonstrated that all three treatments reduced hepatic damage; however, CM had the most significant impact. CM administration led to greater reductions in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), fibrosis-related genes such as alpha-smooth muscle actin (α-SMA) and transforming growth factor beta (TGF-β), and collagen deposition. CM also enhanced the expression of matrix metalloproteinase-12 (MMP-12), promoting extracellular matrix remodeling. Histological analysis confirmed improved liver architecture and reduced fibrosis scores in the CM group compared to Exo and WJ-MSC groups.

Conclusion: In conclusion, our data suggest that WJ-MSC-derived CM provides a more effective, safer, and acellular alternative to MSC and Exo therapy in alleviating liver fibrosis, offering promise for future translational applications.

Keywords: Liver fibrosis, Conditioned Medium, Exosomes, Wharton's Jelly Mesenchymal Stem Cells, Cell-free therapy

Ps-23: Conditioned Medium Outperforms Exosomes and MSCs in Treating Hepatic Fibrosis

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Conclusion: In conclusion, our data suggest that WJ-MSC-derived CM provides a more effective, safer, and acellular alternative to MSC and Exo therapy in alleviating liver fibrosis, offering promise for future translational applications.

Keywords: Liver fibrosis, Conditioned Medium (CM), Exosomes (Exo), Wharton's Jelly Mesenchymal Stem Cells (WJ-MSCs), Cell-free therapy

Ps-24: Comparative Analysis of Gene Expression Changes in the Brain and Blood of ALS Patients

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Objective: Amyotrophic lateral sclerosis (ALS) is a progres-

sive neurodegenerative disease affecting motor neurons in the brain and spinal cord. This study aimed to compare gene expression profiles in brain and blood samples of ALS patients to better understand the disease's underlying molecular pathways.

Materials and Methods: Three microarray datasets (GSE179819, GSE112676, GSE4595) with a total of 741 samples (233 ALS, 508 controls) were obtained from the Gene Expression Omnibus (GEO). Differential expression analysis was performed using R software and the limma package. Pathway and Gene Ontology analyses were conducted via miRTarBase, while protein-protein interaction (PPI) networks were assessed using CytoHubba and MCODE.

Results: In blood samples, 459 genes were differentially expressed, while 157 genes showed significant changes in brain tissue. Neurodegenerative pathways were most enriched in blood, whereas shigellosis emerged as the top pathway in brain samples. Eighteen genes and two microRNAs (miR-1245, miR-342-3p) showed consistent expression changes in both tissues, primarily related to protein binding and innate immune response.

Conclusion: This study contributes to a deeper understanding of ALS molecular pathways and highlights potential biomarkers and therapeutic targets through the identification of common gene expression changes and microRNAs in brain and blood samples.

Keywords: Gene Expression, ALS, Brain, Blood

Ps-25: Clove Extract Loaded on Chitosan Hydrogel Promotes Fibroblast Differentiation of Mesenchymal Stem Cell

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Objective: In recent decades, there has been considerable interest in developing and manufacturing wound dressings that can regenerate and repair skin tissue. The objective of this project is to incorporate clove extract into a composite hydrogel consisting of polyvinyl alcohol (PVA) and chitosan (CS) for application as a wound dressing.

Materials and Methods: The PVA/CS hydrogel containing clove extract (CE) was prepared using a freeze-dryer. Its property was evaluated using scanning electron microscopy (SEM). The biocompatibility of the PVA/CS/CE hydrogel and cell adhesion to the hydrogel using adipose-derived mesenchymal stem cells (ADMSCs) were investigated through the MTT test for 24h. Immunocytochemistry assays were used to investigate the expression of Coll protein.

Results: SEM imaging of the hydrogel's cross-section revealed an interconnected and porous structure. Culturing ADMSCs in proximity to the prepared hydrogel confirmed its biocompatibility, promoted proliferation, and induced expression of type 1 collagen protein.

Conclusion: Based on the obtained results, it can be expected that the designed hydrogel structure containing CE has the ability to support the process of fibroblastic differentiation.

Keywords: Hydrogel, Collagen type 1, chitosan, clove extract, fibroblastic differentiation

Ps-26: PIAS Targeted with Five Chemical Molecules as A Possible Transcription Factor Has Role in Hippocampus Region in Alzheimer's Disease

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Objective: Alzheimer's disease identified as major neurodegenerative disease in our world. The problem has still remained without definite treatment, these circumstances depend on molecular knowledge, which does not cover all aspects of this type of dementia. So, Our solution is to expand our knowledge using high-throughput techniques in a whole-genome study.

Materials and Methods: The authors starting to reanalyze GSE150696 accession dataset from Gene Expression Omnibus (GEO) database. To explore differential expressed genes (DEGs) GEO2R software, to evaluate upstream regulators the ChEA database via the EnrichR web-based tool has been utilized. To specify targeting step, we used Protein Data Bank (PDB) database to evaluate candidate protein by Molegro Virtual Docker (MVD).

Results: In this way, from 2355 up-regulated genes, 14 transcription factors (TFs) identified as have role in AD process in hippocampus region against healthy mouse. More evaluation report that, the PIAS1 has not been reported till now in literature so it is candidate for therapeutic targeting in AD condition. Plus, in five chemical molecule SB-228357, Nitazoxanide, Gabapentin, clofarabine, Bergapten identified as inhibitor of PIAS1.

Conclusion: In this study, we try to expand our molecular knowledges of hippocampus of AD, in this way PIAS1 recognized as TFs in this process which could be targeted by SB-228357, Nitazoxanide, Gabapentin, clofarabine and Bergapten chemical component. The results of this study should be evaluated in wet-lab techniques to be study more as a potential molecular therapy in AD.

Keywords: Docking, PIAS1, Alzheimer's Disease, Bioinformatics, Molecular Docking

Ps-27: Protective Effects of Aloe Vera-Derived Extracellular Vesicles Against UV-B Induced Oxidative Stress in Human Dermal Fibroblasts

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Objective: Exposure to ultraviolet B (UV-B) radiation is a major environmental factor responsible for skin damage, as it triggers oxidative stress, inflammatory responses, DNA damage, and premature aging. Given the rising prevalence of UV-related skin disorders, there is growing interest in natural agents with antioxidant and protective properties. Aloe vera, a plant renowned for its medicinal uses, produces extracellular vesicles (EVs) enriched with proteins, lipids, and microRNAs that may modulate cellular repair mechanisms. This study aims to develop a UV-B induced photoaging model in human dermal fibroblasts (HDFs) and investigate the protective potential of Aloe vera-derived EVs.

Materials and Methods: EVs were isolated from Aloe vera gel using differential centrifugation and characterized by scanning electron microscopy (SEM), dynamic light scattering (DLS) for size distribution, and Western blotting. To determine the optimal UV-B dose for inducing oxidative stress, HDFs were exposed to varying UV-B radiation levels, and intracellular reactive oxygen species (ROS) levels were quantified using a fluorometric microplate assay. The cytotoxicity of Aloe vera-derived EVs was assessed via MTS assay across a range of concentrations on non-irradiated HDFs.

Results: The results confirmed the successful isolation of Aloe vera EVs, with SEM, DLS, and Western blotting validating their structural integrity. ROS levels increased with prolonged UV-B exposure, allowing the selection of an appropriate irradiation dose for cellular modeling. The MTS assay revealed no cytotoxicity for Aloe vera EVs, as evidenced by the IC50 value. Subsequent studies will evaluate the rejuvenating effects of these isolated EVs on UV-B induced senescent fibroblasts, focusing on cellular repair mechanisms and markers of skin aging.

Conclusion: This study successfully established protocols for Aloe vera EV isolation and developed a UV-B induced oxidative stress model in HDFs. Future research will explore the therapeutic potential of these EVs in reversing UV-B induced damage, focusing on antioxidant activity, collagen synthesis, and inflammatory markers.

Keywords: Extracellular vesicles, Human dermal fibroblasts, Aloe vera, Oxidative stress, Ultraviolet rays

Ps-28: Epidermal Stem Cells Transplantation Prevents Memory Impairment Induced by Streptozotocin Via Modulation of Inflammatory Markers and Antioxidant Activity

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Objective: Alzheimer's disease (AD) is the most common form of dementia, characterized by progressive neural cell loss, neurodegeneration, and inflammation, leading to cognitive decline and memory impairment. Given the pivotal role of inflammation in AD pathogenesis, neuroprotective strategies are critically needed. Epidermal stem cells (EPI-SCs) have shown promise in cell-based therapies due to their ability to differentiate into neural cell types and their migratory and restorative potential observed in preclinical models. This study aimed to evaluate the therapeutic effects of EPI-SCs transplantation on cognitive function and inflammatory responses in streptozotocin (STZ)-

induced rats, a model mimicking AD pathology.

Materials and Methods: Adult male Sprague-Dawley rats (250–300 g) were divided into control, STZ, and STZ+EPI-SCs groups. The rats underwent stereotaxic surgery and STZ (3 mg/kg) was intracerebroventricularly injected, followed by EPI-SC transplants (1×10^6) on days 4, 14, and 21 post-surgery. Memory was assessed via passive avoidance test. Hippocampal tissues were analyzed for inflammatory cytokine mRNA expression using quantitative RT-PCR. Further, the level of malondialdehyde (MDA) in hippocampal tissue was quantified as a marker of oxidative stress.

Results: The STZ significantly impaired memory, evidenced by decreased step-through latency ($P < 0.05$), while EPI-SC treatment notably improved cognitive performance ($P < 0.05$). Elevated hippocampal levels of TNF- α , IL-1 β , and IL-6 observed in the STZ group were markedly reduced following EPI-SCs transplantation ($P < 0.001$), indicating an anti-inflammatory effect of EPI-SCs. Additionally, oxidative stress was heightened in the STZ group compared to the control group, with increased MDA levels ($P < 0.01$), which were significantly attenuated by EPI-SCs ($P < 0.01$), suggesting antioxidant activity.

Conclusion: EPI-SC transplantation exerts neuroprotective effects in an AD model by improving cognitive deficits, reducing inflammation, and mitigating oxidative stress. These findings support the potential of epidermal stem cells as a promising therapeutic strategy for AD.

Keywords: Stem cells, Alzheimer Disease, Streptozotocin, Memory, Inflammation

Ps-29: Assessing the Protective Effects of EGF in Human Dermal Fibroblasts Against UV-B-Induced Photoaging and Oxidative Stress

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Objective: UV-B radiation penetrates the epidermis and generates reactive oxygen species (ROS), a key contributor to skin aging. Elevated ROS levels activate matrix metalloproteinases (MMPs), leading to collagen degradation. Epidermal growth factor (EGF), through the EGF/EGFR pathway, promotes cell proliferation and tissue repair, showing potential in reducing oxidative stress. This study evaluates EGF's protective effects against UV-B-induced damage in human dermal fibroblasts (HDFs).

Materials and Methods: In this study, HDFs were treated by progressive doses of UV-B irradiation to determine the minimum dose that effectively induce oxidative stress. Then, intracellular ROS generation was evaluated using the ROS Kit by fluorometric method. At the same time, different concentrations of EGF (produced at the Royan Institute) were applied to HDFs, and cytotoxicity was assessed through MTS assay to determine the IC50 value. These optimization steps provide the

baseline for the following experiments.

Results: Initial data have shown increases in ROS following UV-B exposure, allowing for the selection of a suitable dose to induce oxidative stress. Also, IC₅₀ of EGF on HDFs was shown 22 ng concentration of this recombinant protein required to preserve cell viability while enabling biological activity.

Conclusion: The optimized UV-B and EGF dosing parameters presented a robust in vitro model. Upcoming experiments will assess the impact of EGF on reducing oxidative stress and regulating the expression of key genes involved in extracellular matrix remodeling, including COL1A1, MMP1, 3, and TGFβ in modeled HDF cells through UV-B rays.

Keywords: Recombinant EGF^r (rhEGF), UV-B (Ultraviolet-B), Oxidative Stress, Skin Photoaging, Human Dermal Fibroblasts (HDFs)

Ps-30: Anti-Alzheimer's Potential of Royal Jelly: Antioxidant Properties, Cholinesterase Inhibition, and In Silico Studies

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Objective: Alzheimer's disease (AD) is a chronic, progressive neurodegenerative disorder and the most common cause of dementia worldwide, primarily affecting the elderly population. It is clinically manifested by memory impairment, cognitive dysfunction, and behavioral disturbances, which significantly impact patients' quality of life. The pathological hallmarks of AD include the accumulation of amyloid-beta (Aβ) plaques, hyperphosphorylation of tau proteins leading to neurofibrillary tangles, cholinergic neuron degeneration, and increased oxidative stress in the brain. Despite extensive research, current therapeutic options remain limited and largely symptomatic, highlighting the urgent need for more effective and safer interventions. Natural products, particularly those with antioxidant and neuroprotective properties, have gained increasing attention as potential alternatives. Royal jelly (RJ), a secretion produced by honeybees, has shown promising biological activities, including antioxidant, anti-inflammatory, and cholinesterase inhibitory effects, which may counteract key pathological mechanisms in AD. In this study, we aimed to investigate the antioxidant potential, cholinesterase inhibition, and molecular docking interactions of RJ bioactive components with AD-relevant targets, providing new insights into its therapeutic potential in Alzheimer's disease.

Materials and Methods: Royal jelly samples were sourced from certified suppliers and lyophilized for uniformity. Antioxidant capacity was assessed using the TEAC radical-scavenging assay, with absorbance measured at 734 nm. Results were expressed as IC₅₀ values (mg/mL). Enzyme inhibition studies targeted acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) using Ellman's method, wherein hydrolysis of acetylthiocholine iodide and butyrylthiocholine iodide was monitored spectrophotometrically at 412 nm. The inhibitory concentrations were determined in triplicates for accuracy. For in silico analyses, major bioactive components of RJ—10-hydroxy-2-decenoic acid (10-HDA) and Major Flavonoids

—were identified via published databases. Molecular docking was conducted using schrodinger suites software against AChE and BuChE. Ligand-protein interactions, binding affinities, and key residues involved in stabilization were analyzed and visualized with PyMOL. MD(Molecular Dynamics) simulations were conducted using Desmond to assess the stability of ligand-AChE/BuChE complexes. RMSD, RMSF, and protein-ligand interactions were analyzed to evaluate binding stability and conformational changes.

Results: RJ exhibited antioxidant activity with an IC₅₀ value of 70 mg/mL, demonstrating its potential to neutralize free radicals. Cholinesterase inhibition tests revealed a dose-dependent suppression of enzymatic activity, with a maximum inhibition of 40% for acetylcholinesterase and 35% for butyrylcholinesterase at a concentration of 200 µg/mL. Molecular docking showed that RJ components like 10-HDA, isorhamnetin 3-O-glucoside, Acacetin, Chrystin and Formononetin formed stable interactions with key binding sites of acetylcholinesterase and butyrylcholinesterase with -10.261 and -9.253 binding energies.

Conclusion: These findings emphasize RJ's potential as a multi-target therapeutic agent for AD by mitigating oxidative stress, inhibiting cholinesterase activity, and directly interacting with pathological targets. Further preclinical studies are warranted to translate these effects into clinical benefits.

Keywords: Royal jelly, acetylcholinesterase, antioxidant activity, 10-HDA, in silico docking

Ps-31: Fast Production of CD19 CAR T Cells Preserves Phenotype and Enhances Functional Fitness Compared to Conventional Production

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Objective: Chimeric Antigen Receptor (CAR) T cell therapy has emerged as a breakthrough in the treatment of hematological malignancies. However, conventional ex vivo manufacturing protocols are often lengthy and resource-intensive, which can lead to increased T cell differentiation, ultimately diminishing long-term persistence and therapeutic efficacy. These limitations have driven extensive efforts, both in academic research and industry, to optimize and refine CAR T cell production strategies.

Materials and Methods: In this study, we developed a modified manufacturing protocol aimed at preserving a less-differentiated, functionally potent T cell phenotype. The revised process significantly reduces the interval between T cell activation and viral transduction to under 24 hours. It shifts a considerable portion of cellular expansion from in vitro culture to the in vivo environment, thereby decreasing overall culture duration and potentially enhancing physiological relevance.

Results: We conducted a direct comparison between CAR T cells generated via this fast protocol (FT-CARaCell19) with those from produced through a conventional 10–12 day process (CT-CARaCell19). Analytical endpoints included CAR expres-

sion levels, CD4/CD8 T cell ratio, and subset distribution, all evaluated via multicolor flow cytometry. Additionally, rapid-release quality control assays—such as identity confirmation, phenotypic purity, and surface CAR expression quantification—were employed to ensure compliance with essential product standards. Despite the shortened ex vivo processing time, FT-CARaCell19 demonstrated comparable and in some aspects superior, characteristics relative to CT-CARaCell19. Key findings included balanced CD4/CD8 ratios, robust CAR surface expression, and enrichment of less-differentiated T cell subsets within minimal expression of exhaustion markers. All quality parameters, including cell viability and purity, met clinical-grade release criteria.

Conclusion: These findings suggest that strategic modifications to the manufacturing timeline can effectively preserve critical T cell qualities while streamlining the production process. This approach offers a promising alternative to conventional protocols, with advantages in scalability, time efficiency, and clinical relevance, without compromising product quality.

Keywords: CAR T cell, Fast Manufacturing, Quality Control, CD4/CD8 T Cell Ratio

Ps-32: Investigating The Role of Podocytes in the Formation of Kidney Organoids in The Presence of Human Umbilical Cord Blood Serum

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Objective: Chronic kidney disease (CKD) poses a growing global health burden, with limited regenerative treatment options. Kidney organoids have emerged as promising tools for modeling nephrogenesis and kidney disorders, yet challenges such as the use of fetal bovine serum (FBS), insufficient structural maturation, and limited clinical translatability hinder their application. To overcome these limitations, we established a novel protocol integrating podocytes-key glomerular cells involved in filtration-with renal progenitor cells in a co-culture system. Additionally, we substituted FBS with human umbilical cord blood serum (hUCBS), a more ethically acceptable and clinically relevant supplement, aiming to enhance organoid functionality and applicability.

Materials and Methods: Clonal renal epithelial and mesenchymal progenitor cells were isolated from mouse kidneys and cultured with podocytes and human umbilical vein endothelial cells (HUVECs) in nephrogenic medium containing hUCBS. Initial observations showed the formation of cell aggregates. Validation of the organoid model using qRT-PCR for wt1, Podx, Nphs1, Aqp1, E-cadherin, Umod, CD34, Aqp2, Gata3, Pdgfrb, protein and histological methods was performed.

Results: Initial findings of qRT-PCR, flow cytometry, and histology showed greater cell aggregation and vascular-like structures in the hUCBS group with the presence of podocytes compared to the FBS group without the presence of podocytes.

Conclusion: This study introduces a novel strategy for generating renal organoids by incorporating podocytes into a co-culture system and utilizing hUCBS as an ethical and effective alternative to fetal bovine serum. This approach addresses both the ethical limitations and the structural immaturity observed in previous models. Nonetheless, further research is required to optimize nephron-specific differentiation and promote angiogenesis.

Keywords: Kidney organoid, podocyte, human umbilical cord blood serum, nephrogenesis, regeneration

Ps-33: Generation HUVEC – GFP Line by Over-expression of hTERT

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Objective: Human umbilical vein endothelial cells (HUVECs) are a widely used in vitro model for endothelial biology but have a limited lifespan due to their embryonic and venous origin, requiring frequent, time-consuming, and costly isolations. To overcome these limitations, we enhanced HUVEC proliferative capacity by upregulating human telomerase reverse transcriptase (hTERT), aiming to extend their lifespan and improve their utility in research.

Materials and Methods: In this study, two groups were examined: a control group and an hTERT group. To this end, primary HUVECs were transfected with a lentiviral vector containing the hTERT and GFP gene sequence to generate a population of HUVECs with enhanced proliferative capacity and traceable in the hTERT group. To confirm the identity of the cells used in both groups, the expression of the endothelial-specific marker CD31 was evaluated. Additionally, to assess the level of hTERT gene expression, qRT-PCR was performed. Finally, to measure the cellular proliferation capacity in both groups, the expression of the proliferation marker Ki-67 was analyzed.

Results: hTERT-transfected HUVECs showed significantly increased hTERT expression and telomerase activity by qRT-PCR. These cells exhibited enhanced proliferation and sustained growth at higher passages while maintaining endothelial marker CD31 expression. Elevated Ki-67 levels further confirmed increased proliferative capacity. These results demonstrate that hTERT overexpression effectively extends HUVEC lifespan without altering cellular phenotype.

Conclusion: This study shows that hTERT transfection in HUVECs significantly increases hTERT expression and telomerase activity, enhancing proliferation and extending cell

lular lifespan. GFP expression enabled cell tracking. Treated cells retained endothelial marker CD31, confirming phenotype preservation, while elevated Ki-67 levels indicated increased proliferation. These results support hTERT overexpression as an effective strategy to overcome HUVEC lifespan limitations, enabling longer-term endothelial research.

Keywords: HUVECs, hTERT, Telomerase, Passagability

Ps-34: Next-Gen Exosome Tech: A New Era in Rapid, Precise, and Label-Free Liquid Biopsy

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Objective: Exosomes represent nanosized extracellular vesicles that function as essential communication agents while serving as potential biomarkers in liquid biopsies for cancer detection and other disease diagnostics. The intricate nature of traditional isolation methods, combined with their limited output and scalability, restricts their potential for clinical use. Effective management of these challenges demands the development of cutting-edge platforms that deliver high-throughput exosome isolation together with molecular profiling while remaining cost-effective.

Materials and Methods: This investigation integrates multiple microfluidic and acoustofluidic approaches to enhance exosome isolation and detection methods. Researchers utilize antibody-functionalized microbeads in hydrodynamic traps, PDMS-based ExoChip featuring CD63 affinity, acoustically driven disc rotation (ASCENDx), and viscoelastic flow sorting. These platforms employ label-free and contact-free methods alongside antibody-based capture techniques and support downstream applications including fluorescence quantification, Raman scattering, Western blotting, and microRNA profiling.

Results: The performance of all methods for exosome capture and biomarker detection proved robust. The ASCENDx disc attained exosome enrichment at a 95.8% sensitivity rate and 100% specificity for colorectal cancer detection. ExoChip demonstrated that exosome concentrations in pancreatic cancer patients exceeded double those in healthy individuals. Viscoelastic flow microfluidics achieved >97% purity and over 87% recovery from whole blood, surpassing ultracentrifugation. Acoustofluidic devices enabled >99.999% blood cell removal while maintaining >98% exosome purity. The microbead trapping device facilitated single-particle fluorescence quantification and molecular analysis on-chip.

Conclusion: These advanced platforms transform exosome isolation and detection through quick, scalable, label-free, and cost-effective workflows. They offer high precision and clinical adaptability, positioning them as powerful tools for diagnostics, precision medicine, and real-time disease monitoring.

Keywords: Exosome Isolation, Microfluidic Platform, Liquid Biopsy, Biomarker Detection, Label-Free Diagnostics

Ps-35: Organoid Intelligence and Biohybrid Robots: Shaping the Future of Biocomputing and Neurotherapeutics

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Objective: Organoid Intelligence (OI) refers specifically to an innovative discipline that fuses brain organoids, as brain cells grown in a lab that simulate different cell types found in the human brain, with cutting-edge computing and robotics. These models mimic human brain functions, offering promise for medicine and computing. Despite numerous benefits, such developments create a range of ethical, legal, and social problems that require immediate attention and careful management.

Materials and Methods: The most recent biohybrid system was bioinspired from human biology with the combination of cerebral organoids, motor neuron spheroids and skeletal muscle tissue on a microfluidics platform. Real-time electrophysiological recording and artificial learning of the stimulus-response data are the major functions of the 3D cell culture of the human brain and the microfluidic perfusion system.

Results: One of the new applications employs the use of mid-brain organoids developed from the patient, residing in a biohybrid robot-on-a-chip that responds to the treatment of Parkinson's disease medication (levodopa), showing an increase in muscle bundle movement from $4.5 \pm 0.99 \mu\text{m}$ to $18.67 \pm 2.25 \mu\text{m}$. Other applications of OI include a case where a completely digital system is able to perform tasks such as continuous learning, quick decision-making and energy-efficient computation, at the same time energy generation in the form of bioelectricity. With these discoveries, OI is a technology that enjoys a two-fold purpose: for disease modeling and biological computing, especially in cases where a rate of neurogenesis is used as a measure of neurodegenerative diseases.

Conclusion: If it is developed properly and the government is ethical, then the organoid intelligence can become the most important tool in the biomedical and AI sectors. It not only provides us with new ways to understand and fight diseases but also helps us see a new face of computing through "intelligence in a dish". Through the promotion of interdisciplinary collaboration and the participation of the public, OI and biohybrid systems can play an important role in enabling radical applications in the fields of healthcare, robotics, and sustainable technology.

Keywords: Organoid Intelligence (OI), Biohybrid Robot-on-a-Chip, Brain Organoids, Neurodegenerative Disease Modeling, Biocomputing

Ps-36: Regulation of IL-6 and IL-1 β Gene Expression by Vitamin D in a Co-Culture Model of Peripheral Blood Mononuclear Cells and Mesenchymal Stem Cells

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Objective: Peripheral blood mononuclear cells (PBMCs), which produce proinflammatory cytokines such as IL-6 and IL-1 β , play a crucial role in sustaining inflammation. Stem cells (MSCs) have been implicated as immunomodulators that can

reduce inflammatory responses by interacting with immune cells. Vitamin D also suppresses the expression of proinflammatory cytokines and enhances anti-inflammatory pathways. Furthermore, the combined effects of vitamin D and MSCs on the expression of inflammatory genes such as IL-6 and IL-1 β have not been investigated.

Materials and Methods: For the isolation of PBMCs, whole blood samples were collected from 5 healthy donors. PBMCs were added to MSCs at a ratio of 1:1. In the next step, the effects of vitamin D at different concentrations (0, 6, 12, 25, 50, 100 nM) on the gene expression of IL-6 and IL-1 β in the mixture of PBMCs co-cultured with MSCs were determined. To do this, total RNA was extracted. After cDNA synthesis, the expression of the IL6 and IL1 β genes was assessed with Real-time PCR.

Results: The results show that the gene expression of inflammatory cytokines was decreased compared to the control. The mRNA expression level of IL6 was significantly reduced at 6 ($p < 0.001$), 12 ($p < 0.0001$), and 25 ($p < 0.0001$) nM vitamin D concentrations. In addition, the results show that the mRNA expression level of IL1 β cytokine was significantly decreased at 6 ($p < 0.05$) 12 ($p < 0.0001$), 25 ($p < 0.0001$), and 50 ($p < 0.01$) nM vitamin D concentrations compared to the control.

Conclusion: This study suggests that vitamin D plays an essential role in modulating inflammatory responses in a co-culture model of PBMCs and MSCs. Further research is warranted to elucidate the underlying molecular mechanisms and investigate their clinical relevance in immune regulation.

Keywords: Vitamin D, IL-6, IL-1 β , Anti-inflammatory, Mesenchymal Stem Cells

Ps-37: Cancer Stem Cells and EMT: Mechanisms Linking Stemness to Metastasis

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Objective: Secondary tumor development marks the major cause of death due to cancer. The development of metastasis depends highly on epithelial-mesenchymal transition (EMT) because this process ties closely to cancer stem cell (CSC) biological mechanisms. Heterogeneous tumors proliferate to resist treatment because of the self-renewal properties and differentiation potential that CSCs possess. EMT causes epithelial cells to transform into mesenchymal phenotypes resulting in improved cell movement ability for tissue invasion. OTCM functions in two ways to both establish new CSC states and maintain their durability making it a direct pathway between stem cell attributes and metastasis. **Objective:** This research analyzes the cellular pathways between CSCs and EMT together with strategies aimed at treating the shared signaling pathways.

Materials and Methods: The search for relevant literature utilized combinations of Scopus with ScienceDirect and Google Scholar and PubMed databases between the years 2020 and 2025. Researchers utilized the search criteria of Cancer Stem Cells and EMT and Metastasis and Signaling Pathways during their study. A total of three studies within seven selected articles studied the metastasis-EMT-CSCs interaction relationship.

Results: Stemness regulators OCT4 and NANOG together with SOX2 maintain invasive behavior by creating binding associations with transcription factors ZEB1, TWIST and SNAIL. Three EMT-related markers can be detected in CSCs which contain CD44-positive CD24-negative profiles as well as ALDH and CD133. EMT and stemness maintenance result from simultaneous Wnt/ β -catenin and TGF- β signaling activation. Research confirmed that the natural compounds curcumin and quercetin-3-methyl ether could block EMT and CSC pathways through their ability to interrupt Wnt pathway and Notch signaling and PI3K/Akt signaling cascade.

Conclusion: EMT and CSCs communicate through identical molecular procedures to support the metastatic process. The therapies that target their interaction process present an innovative treatment method. Complex tumors could be restrained by using specific drug inhibitors in concert with different natural compounds.

Keywords: Cancer Stem Cells, EMT, Metastasis, TGF- β , Stemness

Ps-38: Isolation and Characterization of Human Newborn Foreskin Stem Cells

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Objective: Pluripotent stem cells have been isolated from various tissues and utilized in cell therapy. Recently, the skin has emerged as a promising source for these cells. Epidermal stem cells are fundamental to cellular regeneration, wound healing, and neoplasm formation. Their ability to undergo reprogramming and differentiation into other cell types offers new prospects in regenerative medicine. Consequently, identifying and isolating these cells is of vital importance.

Materials and Methods: Human foreskin tissue was obtained from newborns undergoing circumcision. Cells were isolated using dispase and trypsin enzymes. The isolated cells were then transferred onto culture surfaces coated with fibronectin and laminin and cultured in a medium containing serum treated with Chelex-100. Following the observation of cell colonies, growth factors were added to promote cell proliferation. Cells were passaged after homogenization. The expression of epidermal stem cell-specific markers in the isolated cells was examined via immunofluorescence and flow cytometry. Additionally, alkaline phosphatase activity and the differentiation potential toward osteogenic, adipogenic, and neural lineages were evaluated.

Results: Immunofluorescence analysis confirmed the expression of human epidermal stem cell markers, including beta-1 integrin and CD49f. Flow cytometry at passage 3 indicated that 42% of the cells expressed beta-1 integrin and 31% expressed CD49f, whereas the expression of the marker CD71 was minimal. Differentiation into osteogenic lineage was verified by Alizarin Red staining, adipogenic differentiation was confirmed with Oil Red O staining, and neural differentiation was demonstrated through Cresyl violet staining, indicating the multipotent potential of these cells.

Conclusion: The results of our study demonstrated that the skin harbors stem cells capable of differentiating into various cell types under appropriate conditions, suggesting their potential as a valuable source for regenerative cell therapy

Keywords: Human Newborn Foreskin, Epidermal Stem Cells, Stem Cell Isolation, Stem Cell Differentiation

Ps-39: Heparinized ECM-Based Scaffolds with Platelet-Rich Plasma for Enhanced Skeletal Muscle Regeneration

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Objective: The efficacy of platelet-rich plasma (PRP) in enhancing muscle regeneration has been extensively studied. However, the insufficient PRP regeneration efficacy raises concerns due to its uncontrolled delivery. Considering the widespread use of decellularized scaffolds derived from extracellular matrix (ECM) for muscle regenerative therapy, the loading of PRP growth factors to these scaffolds through heparin affinity can help to overcome this challenge. Therefore, this study focuses on decellularized skeletal muscle ECM-based scaffolds modified with heparin, loading with PRP, with the aim of enhancing endogenous cell recruitment in muscle regeneration.

Materials and Methods: Fresh bovine skeletal muscle tissue was decellularized and then a macroporous sponge scaffold was fabricated from ECM. Subsequently, the scaffold was covalently modified with heparin and treated with PRP. The study focused on the comparative analysis of platelet-derived growth factor and fibroblast growth factor release from both heparin-bound and non-heparinized scaffolds over time in vitro. Additionally, the impact of these factors on the proliferation and differentiation of C2C12 cells was investigated. In a mice model of volumetric muscle loss, the implanted scaffolds were evaluated for angiogenesis and the infiltration of muscle cells.

Results: Our findings indicated an optimal decellularization procedure that effectively removed cells while preserving the ECM components in skeletal muscle tissue. The macroporous scaffolds showed suitable physical and mechanical properties for muscle tissue engineering. Regarding the release of growth factors from PRP, the heparin-conjugated scaffold demonstrated a more sustained release of PDGF-BB and FGF over two weeks. As a result of this sustained release from PRP, the metabolic activity of C2C12 cells in heparinized scaffolds was significantly increased. Notably, this scaffold also promoted myogenic differentiation of C2C12 within the scaffold which was confirmed by RT-qPCR. In the VML model, histological analysis of implanted scaffolds after one month revealed higher angiogenesis and more extensive migration of host muscle cells within heparin-conjugated scaffolds.

Conclusion: The heparinized scaffold facilitated the attraction and sustained release of growth factors from PRP, which in turn promoted the recruitment of endothelial and native muscle cells to the injured tissue. These findings have the potential to enhance the accessibility of decellularized scaffolds for off-the-shelf use and hold promise for treating substantial muscle defects in clinical practice.

Keywords: Tissue engineering, Muscle regeneration, Extracellular matrix, Platelet-Rich Plasma

Ps-40: Enhancing Regeneration of Amputated Mouse Digit Tips Using TAK-242 and Bone Marrow-Derived Mesenchymal Stem Cells

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Objective: Digit amputation significantly impairs quality of life, and unlike regenerative amphibians, adult mammals exhibit limited limb regeneration due to persistent inflammation and fibrotic scarring. Although mesenchymal stem cell (MSC) therapy holds promise for tissue regeneration, its efficacy remains constrained by the inflammatory microenvironment. TAK-242, a selective inhibitor of Toll-like receptor 4 (TLR4), has been shown to attenuate inflammation. This study investigates the combined effect of TAK-242 and human bone marrow-derived MSCs (hBM-MSCs) on the regeneration of amputated digit tip in a murine model.

Materials and Methods: Adult C57BL/6 mice underwent digit amputation at the distal phalanx of digits 2-4 to establish a regeneration model. hBM-MSCs were cultured and characterized under standard conditions. The cytotoxicity of TAK-242 was confirmed using MTS assay. Subsequently, 5–7×10⁵ hBM-MSCs and 100 nM TAK-242 were embedded in 5 µL hydrogel (HG) and locally administered to the amputation site. Experimental groups included TAK-242/HG, MSCs/HG, TAK-242/MSCs/HG, and Sham, with comparisons made against untreated and intact control groups. After 8 weeks, regenerative outcomes were evaluated through macroscopic observation and histological analysis.

Results: Characterization of hBM-MSCs confirmed their mesenchymal identity based on spindle-shaped morphology and their capacity to differentiate into adipogenic and osteogenic lineages. The MTS assay demonstrated that 100 nM TAK-242 did not compromise hBM-MSC viability. After 8 weeks, macroscopic observations revealed digit elongation and new nail regrowth in the HG/TAK-242/MSCs group, which was not observed in other treatment groups. Histological analysis using H&E and MT staining further confirmed the formation of new bone, connective tissue, and nail structures in this group. In contrast, the TAK-242/HG and MSCs/HG groups displayed abnormal tissue formation, while the sham group had no evidence of regenerative tissue development.

Conclusion: These findings suggest that the combination of MSCs and TAK-242 may promote structural regeneration by

modulating the inflammatory response and creating a pro-regenerative microenvironment

Keywords: Digit tip regeneration, Mesenchymal stem cells, TAK-242, TLR-4

Ps-41: Metformin Up-regulated the Expression of Genes Involved in Extracellular Vesicle Biogenesis

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Objective: Extracellular vesicles (EVs) from colorectal cancer (CRC) cells contribute to the growth, invasion, and progression of CRC. Metformin, an anti-diabetic drug, has anti-cancer properties in several cancers. We aimed to investigate the expression of genes involved in EVs production in CRC cells.

Materials and Methods: HCT-116 cells were treated with serial doses of metformin for cytotoxic assay for 48 h. We measured the expression of Rab27a and Lamp-2 genes in HCT-116 cells treated with metformin by real-time PCR technique over a period of 48 h.

Results: Our results showed that the IC₅₀ value was 7.5 mM for 48h. Compared to control cells, metformin significantly up-regulated expression of genes, Rab27a and Lamp-2, involved in EV biogenesis and secretion ($p < 0.05$).

Conclusion: Data indicates metformin could promote transcript levels of Rab27a and Lamp-2, suggesting an increase in EVs biogenesis.

Keywords: Extracellular vesicles, Metformin, Rab27a, HCT116, CRC

Ps-42: Royal Jelly loaded in Scaffolds Accelerate Skin Burn Wound Healing in Rats

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Objective: Skin burn wounds pose a substantial challenge for clinicians due to the complex nature of the required treatment to achieve favorable outcomes. The current approaches to wound management often lack the efficiency required to effectively address these challenges. Based on these findings, this study aims to investigate the effectiveness of royal jelly in promoting burn wound healing.

Materials and Methods: The silk fibroin were characterized through fourier transform-infrared, energy dispersive X-ray, and field emission-scanning electron microscopy analyses. Male Wistar rats with second-degree burns were randomly divided into five groups: untreated burns, silver sulfadiazine

(1%), silk fibroin and silk fibroin/royal jelly scaffolds. The various groups underwent a 21-day treatment, during which changes in the wound site were evaluated through macroscopic and microscopic examination.

Results: This royal jelly demonstrated biocompatible properties, making them suitable for enhancing burn wound healing. After 21 days of treatment, the wound closure rate in the silk fibroin /royal jelly group was faster than that of the untreated groups ($p < 0.05$).

Conclusion: The results of this study demonstrate the healing efficacy of silk fibroin /royal jelly as an effective therapeutic approach for the treatment of burn wounds.

Keywords: Wound Healing, Burn, Skin, Royal Jelly

Ps-43: RNA-Sequencing and Network-Based Reanalysis of Tipranavir-Treated Gastric Cancer Stem Cells Reveals Key Signaling Pathways

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Objective: Gastric cancer stem cells (GCSCs) are crucial in tumor progression and resistance to therapy. This study aims to reanalyze RNA-seq data of Tipranavir-treated GCSCs to identify key signaling pathways and central genes involved in Tipranavir's potential therapeutic action.

Materials and Methods: Publicly available RNA-seq data of Tipranavir-treated and control GCSCs (GSE161825) were reanalyzed to identify differentially expressed genes (DEGs) with a fold-change threshold of ± 1 . Protein-protein interaction (PPI) networks were constructed using STRING and visualized in Cytoscape. Centrality analysis identified 58 key genes, with ACTB, ALB, CXCL8, and CCND1 as the most central nodes. Gephi software was employed for clustering and modularity analysis, resulting in four clusters. Enrichment analysis of the cluster containing ACTB revealed key signaling pathways using STRING.

Results: Enrichment analysis identified several significant pathways, including the PI3K-Akt signaling pathway, focal adhesion, ECM-receptor interactions, and integrin cell surface interactions. Notable cancer-related pathways, such as proteoglycans in cancer and PI3K-Akt-mTOR signaling, were highlighted, further supporting Tipranavir's role in disrupting GCSC-associated signaling.

Conclusion: This RNA-seq-based network analysis identified central genes and key signaling pathways targeted by Tipranavir in GCSCs. These findings provide insights into its mechanisms of action and highlight its potential as a therapeutic agent for gastric cancer.

Keywords: Cancer Stem Cells, Gastric Cancer, RNA-Sequencing, Bioinformatics

Ps-44: Vitamin D-induced IL-4 and TGF- β up-regulation in a Co-Culture Model of Peripheral Blood Mononuclear Cells and Mesenchymal Stem Cells

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Objective: Peripheral blood mononuclear cells (PBMCs) are crucial for regulating immune responses by producing anti-inflammatory cytokines like IL-4 and TGF- β . Mesenchymal stem cells (MSCs) are known to have the capability to influence immune function and aid in tissue repair through their immunosuppressive properties. Vitamin D, recognized for its ability to modulate the immune system, can further increase the levels of anti-inflammatory mediators. However, the combined effects of vitamin D and MSCs on IL-4 and TGF- β levels in PBMCs have not yet been investigated.

Materials and Methods: For the isolation of PBMCs, whole blood samples were collected from 5 healthy donors. Then, PBMCs were separated. PBMCs were co-cultured with MSCs at a 1:1 ratio. Subsequently, the effects of varying concentrations of vitamin D (0, 6, 12, 25, 50, and 100 nM) on IL-4 and TGF- β gene expression in the co-culture system were evaluated. Total RNA was extracted, followed by cDNA synthesis, and gene expression levels were quantified using real-time PCR.

Results: The data demonstrated a significant upregulation of IL-4 and TGF- β gene expression in vitamin D-treated groups compared to the control. IL-4 mRNA levels were markedly increased at 12 ($p < 0.05$) and 25 ($p < 0.01$) nM vitamin D concentrations. Similarly, TGF- β expression showed a significant elevation at 6 ($p < 0.01$), 12 ($p < 0.0001$), 25 ($p < 0.001$), and 50 ($p < 0.01$) nM vitamin D doses relative to untreated cells.

Conclusion: The findings of this study show that vitamin D supplementation significantly increases the expression of key anti-inflammatory cytokines IL-4 and TGF- β in PBMCs co-cultured with MSCs. This represents a promising synergistic effect that could be explored in future studies of inflammatory and autoimmune disorders, as well as regenerative medicine.

Keywords: Vitamin D, IL-4, TGF- β , Mesenchymal stem cell, Anti-inflammatory

Ps-45: Optimizing Cryopreservation of Human Embryonic Stem Cells to Comply with GMP Conditions

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Objective: The advent of human stem cell therapies has revolutionized regenerative medicine, emphasizing the importance of reliable cell banking and scalable production processes. A critical challenge in this field is developing cryopreservation methods that comply with Good Manufacturing Practices (GMP), which are mandatory for clinical-grade cell production. Traditionally, fetal bovine serum (FBS) is incorporated into cryopreservation media to protect human embryonic stem cells

(hESCs) during freezing and thawing. However, its use poses significant limitations, including the risk of zoonotic disease transmission, serum variability, ethical concerns, and regulatory hurdles associated with its bovine origin. This study aims to evaluate the efficacy of human serum albumin (HSA)-based cryopreservation in maintaining the integrity, viability, and pluripotency of hESCs. HSA has been used in pharmaceutical formulations, making it suitable for GMP-grade cell processing.

Materials and Methods: We formulated a cryopreservation medium consisting of 50% HSA, 40% normal saline and 10% DMSO, a commonly used cryoprotectant. For controls, cells were frozen in a standard medium of 90% FBS and 10% DMSO. hESCs were cultured under standard conditions and then cryopreserved in the vapor of liquid nitrogen at -196°C. The cryopreserved cells were evaluated after 1 week, as well as after 1, 3, 6, and 12 months of storage, to determine the long-term stability of the cryopreservation method.

Results: Our data demonstrated that the HSA-based cryopreservation medium effectively preserved hESCs, with viability rates comparable to those preserved with FBS across all time points. Morphologically, the cells retained a typical, undifferentiated pluripotent phenotype. The alkaline phosphatase activity was maintained after thawing. Karyotype analysis confirmed that the cells preserved their genetic stability throughout the storage period. No significant differences were observed in post-thaw growth rates, indicating that the HSA formulation supports the long-term preservation of functional pluripotent cells suitable for clinical use.

Conclusion: Our research confirms that HSA can serve as an effective and safe alternative to FBS in the cryopreservation of hESCs under GMP-grade conditions.

Keywords: Human Embryonic stem cells (hESCs), GMP conditions, Cryopreservation, Human serum albumin (HSA)

Ps-46: Induction of Apoptosis in Gastric and Esophageal Carcinoma Cells Using Polyoxometalate [Mo36] Nanoparticles

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Objective: Polyoxomolybdates (POMs) have gained attention for their biological activity, particularly as anti-cancer agents. This study explores how polyoxomolybdate nanoparticles trigger apoptosis in cancer cells. To improve stability and efficacy in biomedical applications, we synthesized nanoparticulate form of $(\text{NH}_4)_{12}[\text{Mo}_{36}(\text{NO}_4)\text{O}_{108}(\text{H}_2\text{O})_{16}]$ designated as Mo36.

Materials and Methods: The anti-tumor effects of Mo36 nanoparticles (NPs) were evaluated in two widely used human cancer cell lines, AGS (gastric adenocarcinoma) and KYSE30 (esophageal squamous cell carcinoma). Cell viability and apoptotic induction were assessed via MTT assay, crystal violet staining, live-dead staining, and flow cytometry. The effect of Mo36 NPs on key apoptotic markers BCL-2, BAX, and Caspase-3 was examined using qRT-PCR.

Results: Dose- and time-dependent cytotoxicity was observed in both cell lines treated with Mo36 NPs, as demonstrated by MTT, crystal violet, and live-dead assays. The IC₅₀ of Mo36 NPs for AGS cells at 24, 48, and 72 hours was determined to be 382.2, 157.4, and 85.9 $\mu\text{g/mL}$, respectively, while KYSE30 cells exhibited IC₅₀ values of 1165.8, 754.4, and 484.4 $\mu\text{g/mL}$.

over the same time course. Apoptotic induction was confirmed by flow cytometry. qRT-PCR assay revealed that Mo36 NPs modulate apoptotic pathways by down regulating the anti-apoptotic BCL-2 while upregulating the pro-apoptotic BAX and Caspase-3 expression. Furthermore, Mo36 NPs significantly impaired cell migration and colony formation, suggesting additional anti-metastatic effects.

Conclusion: Our study supports the anti-cancer effects of Mo36 NPs, mediated through the induction of apoptosis and suppression of metastatic potential.

Keywords: Cell death, Mo36, Tumor, Apoptosis, Tumorigenesis

Ps-47: Uncovering Therapeutic Targets in Osteoarthritis via Single-Cell RNA-seq and Drug Repurposing Analysis

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Objective: Osteoarthritis (OA) is a common degenerative joint disorder marked by cartilage breakdown, inflammation, and extracellular matrix (ECM) remodeling. Despite its widespread impact, effective disease-modifying treatments are still limited. Single-cell RNA sequencing (scRNA-seq) provides a powerful approach to unravel the cellular and molecular complexity of OA cartilage, facilitating the discovery of new therapeutic targets.

Materials and Methods: In this study, we analyzed publicly available scRNA-seq data from the GSE255780 dataset, comprising 19 knee cartilage samples from OA patients and non-OA controls. Using the Seurat package in R, we performed standard quality control, normalization, and integration to compare gene expression profiles between OA and non-OA groups. Differential expression analysis was conducted across all cells (non-cluster-specific) to identify key genes involved in OA pathology (threshold: $|\log_2FC| > 1$, $p < 0.05$). Protein-protein interaction (PPI) networks for the top differentially expressed genes (DEGs) were constructed using the STRING database and visualized in Cytoscape. Central hub genes were identified using CentiScaPe based on network topology parameters such as degree and betweenness centrality.

Results: Among the significant DEGs, five hub genes—COL1A2, MMP2, COL6A2, TNF, and CXCL12—emerged as central regulators in the OA transcriptomic network. These genes are known to play crucial roles in cartilage ECM disorganization, matrix degradation, and chronic inflammation. Drug repurposing analysis was conducted using the Drug Gene Interaction Database (DGIDB), revealing both FDA-approved and investigational compounds targeting each of the identified hub genes. Cross-validation with existing literature supported the biological and therapeutic relevance of the selected targets.

Conclusion: This integrative scRNA-seq analysis highlights key hub genes driving OA pathogenesis and proposes a panel of repurposable drugs with potential disease-modifying effects. These findings provide a foundational framework for future experimental validation and the development of targeted OA therapeutics.

Keywords: Osteoarthritis, Bioinformatics, Single Cell RNA Sequencing, Inflammation, Cartilage

Ps-48: Artificial Intelligence in Leukemia: A Comprehensive Systematic Review Across Diagnosis, Prognosis, Treatment, and MRD Monitoring in All Major Subtypes

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Objective: Leukemia is a heterogeneous group of hematological malignancies. The disease includes four main subtypes which display different clinical and pathological features. Accurate and timely diagnosis is critical for improving patient prognosis; however, conventional diagnostic methods are often limited by high costs, prolonged processing times, and reliance on specialized clinical expertise. Modern artificial intelligence techniques including machine learning and deep learning have proven effective for medical professionals to diagnose and treat the disease through improved accuracy and efficiency

Materials and Methods: Considering recent advancements in the application of artificial Intelligence Across various aspects of leukemia diagnosis and management, this study reviews 64 original articles selected from the PubMed database following a systematic search. A screening and selection process based on the PRISMA checklist was done using predefined inclusion and exclusion criteria.

Results: Out of the 64 studies, 75% concentrated on using AI for diagnosis, 12.5% were about prognosis, and 6.25% each dealt with treatment and MRD monitoring. Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML) were the types of leukemia used for most of the studies. A majority of the data used in the study were microscopic images (65.6%). CNNs were the top choice among algorithms, as many studies found their results to be over 95% accurate.

Conclusion: The research shows how AI can help clinicians to achieve early diagnosis, personalized treatment design and continuous disease monitoring; however, more clinical studies are needed to verify AI implementation safety in standard leukemia care protocols.

Keywords: Hematology, Leukemia, Artificial intelligence, Machine learning, Disease Management

Ps-49: Scalable Culture Of AD-MSC in a Suspension Bioreactor System: Toward Therapeutic Supernatant Harvesting

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Objective: Mesenchymal stem cells (MSCs), particularly those derived from adipose tissue (AD-MSCs), have shown promise in regenerative medicine. However, challenges in clinical translation, such as safety and regulatory issues, have shifted focus to cell-free approaches like conditioned medium (CM), which contains therapeutic factors and vesicles without the risks associated with live cells. Due to its lower immunogenicity, ease of storage, and consistency, CM is well-suited for clinical applications. Bioreactor systems offer a solution for scaling CM production under standardized conditions. This study aims to develop a scalable method for producing AD-MSC-derived CM as a therapeutic candidate.

Materials and Methods: Human adipose tissue was obtained via lipoaspiration and processed for MSC isolation through enzymatic digestion. Cells were expanded under standard culture conditions and characterized according to ISCT criteria: plastic adherence, surface marker expression (CD90⁺, CD105⁺, CD34⁻, CD31⁻), and trilineage differentiation potential. For bioreactor setup, cell count, medium volume, and stirring speed were optimized. Spheroid formation was evaluated on day 5 through imaging and size measurement. Conditioned medium from 2D and bioreactor cultures was collected on day 5 and analyzed via ELISA to assess paracrine factor expression.

Results: The isolated cells exhibited fibroblast-like morphology and strong adherence to plastic. Trilineage differentiation was confirmed. Flow cytometry showed MSC identity with high expression of CD90 and CD105, and absence of CD34 and CD31. In the bioreactor, compact spheroids formed by day 5. Preliminary ELISA data revealed higher levels of VEGF, PDGF, FGF2, IGF-1, TGF- β 1, and HGF in bioreactor-derived CM compared to 2D cultures, with IL-10 expression varying slightly.

Conclusion: CM derived from AD-MSCs in a bioreactor system shows enhanced regenerative and immunomodulatory factors, highlighting its clinical potential as a scalable, cell-free therapeutic product for companion set-up.

Keywords: Conditioned Medium, Mesenchymal Stem Cells, 3D Culture, Bioreactor

Ps-50: Molecular Mechanism Underlying Viral and Non-Viral Etiologies of Hepatocellular Carcinoma: Identifying Potential Targets for Diagnosis and Therapy

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Objective: Hepatocellular carcinoma (HCC) is a prevalent and lethal liver cancer, primarily associated with viral infections such as hepatitis B virus (HBV) and hepatitis C virus (HCV), as well as non-viral etiologies. Given the limitation of therapeutic and early detection methods, this study was conducted to examine the expression patterns in individuals with HCC, considering both viral and non-viral risk factors

Materials and Methods: This research utilized available microarray datasets (GSE19665, GSE121248, GSE44074, GSE17856, GSE62232, and GSE45050), to identify differentially expressed genes (DEGs) shared among HBV-related, HCV-related, and non-viral HCC. Network analysis of DEGs was performed using Cytoscape, enabling the visualization and characterization of common hub genes across the groups. To further explore the biological significance of these genes, KEGG pathway enrichment analysis was conducted via Enrichr, elucidating the underlying molecular mechanism involved.

Results: The analysis revealed a significant up-regulation of GPC3 and SPARCL1, irrespective of the etiologic factor. Pathway enrichment analysis of DEGs among HBV-related, HCV-related, and non-viral HCC highlighted key pathways associated with HCC progression, including Wnt signaling, PI3K/Akt, p53, and cell cycle regulation. Additionally, findings suggest that SPP1 may be suppressed by SPARCL1, potentially contributing to HCC development. Furthermore, a notable down-regulation of ALB and HNF4a was observed, both of which play critical roles in HCC incidence and liver function regulation.

Conclusion: This study, by recognizing correlations of common gene profile between viral and non-viral cases the pathways involved, provides insights into the molecular mechanisms of HCC, irrespective of its risk factors. These insights may uncover potential targets for biomarkers in the early diagnosis, monitoring, and treatment of individuals with HCC.

Keywords: Hepatocellular Carcinoma, HBV, HCV, Molecular target, GPC3

Ps-51: Effects of Omega-3 Fatty Acids on the Biochemical and histopathological indices of phenobarbital-induced oxidative stress in Wistar Rats

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Objective: Oxidative stress, a major contributor to cellular damage and disease progression, can be induced by drugs such as phenobarbital. Omega-3 fatty acids, known for their antioxidant properties, may mitigate such adverse effects. This study aimed to evaluate the impact of omega-3 on biochemical and histopathological markers in rats exposed to phenobarbital.

Materials and Methods: Forty adult male Wistar rats were divided into four groups: 1) control group, 2) phenobarbital group (80 mg/kg/BW), 3) omega-3 (30 mg/kg/BW), 4) phenobarbital + omega-3. Treatments were administered orally for 30 days. Then, blood samples were analyzed for liver enzymes such as Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP), Alanine Aminotransferase (ALT), kidney function (urea, creatinine), and lipid profile (cholesterol, triglycerides,

High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL). Histopathological studies on liver and kidney tissues were also conducted. Data analysis was performed using one-way analysis of variance (One-way ANOVA), and $p < 0.05$ was considered significant.

Results: Phenobarbital exposure elevated liver enzymes (AST, ALP, and ALT), impaired kidney function (urea, creatinine), and increased cholesterol, triglycerides, HDL, and LDL compared to the control group. Histologically, liver tissue showed degeneration, necrosis, and disorganization of hepatocytes, while kidney tissues revealed glomerular atrophy and tubular damage. Co-administration of omega-3 fatty acids and phenobarbital significantly attenuated phenobarbital-induced adverse effects, as compared to treatment with phenobarbital alone.

Conclusion: Omega-3 showed protective effects against phenobarbital-induced oxidative damage in rats, highlighting its potential role in preserving liver and kidney function under stress conditions.

Keywords: Omega-3, Phenobarbital, Oxidative stress, Histopathology of kidney and liver

Ps-52: Cytotoxic Effects of Titanium Dioxide Nanoparticles and their correlation with SYNGAP1 Gene Expression in Lymphoblastic Cancer in MOLT-4 Cell Lines

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Objective: Titanium dioxide (TiO₂) nanoparticles with their unique physicochemical properties have found widespread applications in biomedical fields. However, investigations have been performed regarding their potential cytotoxic effects, particularly in malignancies such as acute lymphoblastic leukemia. This study aimed to evaluate the cytotoxicity of TiO₂ nanoparticles and their correlation with the expression of the SYNGAP1 gene, a gene involved in cellular signaling and survival in MOLT-4 leukemia cell lines.

Materials and Methods: In this experimental study, MOLT-4 cell lines were divided into 2 groups: 1) control group, 2) TiO₂ group (exposed to a variety of TiO₂ nanoparticle concentrations (0.2, 0.4, 0.6, 0.8, 1 µg/ml). Cytotoxic effects were assessed using the MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide) assay and flow cytometry. In addition, the Gene expression analysis was performed using Real-time PCR to quantify SYNGAP1 mRNA levels. Data were analyzed using GraphPad Prism version 8. One-way analysis of variance (ANOVA) was used to assess differences between groups, and $p < 0.05$ was considered significant.

Results: The results demonstrated that TiO₂ nanoparticles induced a dose- and time-dependent cytotoxicity in the MOLT-4 cells. Furthermore, SYNGAP1 gene expression was significantly ($p < 0.05$) down-regulated in the treated cells compared to the control group.

Conclusion: These findings suggest that TiO₂ nanoparticles possess potential anti-cancer properties by inhibiting the proliferation of MOLT-4 cells, possibly through downregulation of SYNGAP1 Gene. Suppression of this gene may disrupt cellular functions and contribute to the apoptosis of these cancerous cells.

Keywords: Acute lymphoblastic leukemia, Titanium dioxide nanoparticles, MOLT-4 cells, SYNGAP1 gene

Ps-53: Improving The Therapeutic Properties of Human Amniotic Membrane-Derived Mesenchymal Stem Cells and Their Derivatives by Hypoxia Activation

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Objective: Hypoxia is a method used to stimulate stem cells to produce more derivatives, especially exosomes. Enhancing the quantity and quality of exosomes can improve their therapeutic properties. The study aimed to evaluate the effect of normoxic and hypoxic conditions on the total cell count, viability, migration, and differentiation potential of human amniotic membrane-mesenchymal stem cells (AM-MSCs). Additionally, we evaluated the morphological characteristics, structural properties, chemical features, and biocompatibility of exosomes derived from the hypoxia- and normoxia-AM-MSCs.

Materials and Methods: Human mesenchymal stem cells were isolated from the amniotic membrane through a two-step enzymatic digestion and confirmed by flow cytometry. AM-MSCs were propagated under normoxic (22% O₂) and hypoxic (1% O₂) conditions and evaluated for total cell count, viability, migration, and differentiation potential. After extraction of exosomes from both groups via ultracentrifugation, we examined the morphological characteristics (shape, size, distribution, and agglomeration), structural properties (aggregation, homogeneity, colloidal particle behavior, surface charge, and stability), chemical feature (functional groups and ionic interactions), biological capacities (total protein concentration, and cytotoxicity), and biocompatibility (microbiological quality, systemic-toxicity, irritation and sensitization) of exosomes from hypoxia and normoxia conditions.

Results: The study demonstrated that hypoxia did not adversely affect the stemness potential of AM-MSCs ($P > 0.05$). The average size of exosomes derived from AM-MSCs (AM-MSCs-Exo) in the normoxic and hypoxic conditions was 185.7 nm ($PI = 0.756$) and 145.4 nm ($PI = 0.420$), respectively ($P \leq 0.05$). Zeta potential of AM-MSCs-Exo in the normoxic condition was -12.57 ± 0.5 mV, while it was -2.37 ± 0.73 mV in the hypoxic condition. AM-MSCs-Exo in the hypoxic group exhibited more uniformity, dispersion, and stability than those from the normoxic group, resulting in reduced fluctuation over time under scattered light ($P \leq 0.05$). The average total protein concentration in the hypoxic condition was significantly higher than in the normoxic group (4.109 mg/ml vs. 5.003 mg/ml, representing a 1.22-fold increase under hypoxia) ($P \leq 0.01$). Exosomes extracted under normoxic and hypoxic conditions demonstrated acceptable biocompatibility, no cytotoxicity, irritation, sensitivity, and microbial contamination.

Conclusion: Exosomes from hypoxia-AM-MSCs have greater therapeutic potential due to their unique composition and properties.

Keywords: Exosome, Biocompatibility, Hypoxia, Mesenchymal stem cell Amniotic membrane, Amniotic membrane

Ps-54: Anti-Fibrotic Effects of Human Placenta Extract on Activated Hepatic Stellate Cells

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Objective: Liver diseases result in two million deaths annually and pose a significant global health challenge. Anti-fibrotic therapies focus on hepatic stellate cells as the primary fibrogenic cells to alleviate liver fibrosis, a condition that develops following liver diseases in an inflammatory and oxidative environment. Recent progress in biomaterials has introduced promising strategies in regenerative medicine. The decellularized extracellular matrix (ECM) from the placenta has been identified for its antioxidative, anti-inflammatory, and regenerative properties.

Materials and Methods: LX2 cells were activated with TGF β for 24 hours, followed by treatment with human placenta extract for an additional 24 hours. Cell cycle analysis was performed using flow cytometry. The expression of fibrogenic-related proteins and intracellular reactive oxygen species (ROS) levels were assessed. Additionally, mRNA expression levels of extracellular matrix (ECM) components and oxidative stress-related genes were analyzed. Cell migration was evaluated through a collagen contraction assay, and the mRNA expression of epithelial-mesenchymal transition (EMT)-related genes was determined.

Results: Human placenta extract attenuate hepatic stellate cell activation through regulating the ROS accumulation, ECM expression, and cell migration.

Conclusion: Biomaterials derived from the placenta show potential as a promising treatment for reducing fibrogenic factors associated with liver fibrosis. These innovative placental biomaterials offer a hopeful avenue for addressing the underlying mechanisms contributing to liver fibrosis and may pave the way for more effective therapeutic interventions in this challenging condition.

Keywords: Liver fibrosis, Hepatic stellate cell, Biomaterials, Regenerative medicine

Ps-55: In Silico Transcriptomic Analysis of Peripheral Blood Mononuclear Cells in Primary Sjögren's Syndrome: Identifying Therapeutic Targets for MSC-Derived Exosome-Mediated Immune Regulation

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Objective: Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by exocrine gland dysfunction,

inflammation, and fatigue, often leading to reduced quality of life. Mesenchymal stem cell (MSC)-derived exosomes have shown promise in modulating immune responses in autoimmune conditions through their immunosuppressive and regenerative properties. This study aims to identify transcriptomic biomarkers in peripheral blood mononuclear cells (PBMCs) of pSS patients that may serve as therapeutic targets for MSC-derived exosome-based interventions.

Materials and Methods: Two publicly available RNA-Seq datasets (GSE199868 and GSE145065) were analyzed. From each dataset, three healthy controls and three pSS samples were randomly selected. Raw sequencing data were downloaded from the SRA database and processed using the Galaxy platform. Genes with adjusted p-values < 0.05 and |log₂(FC)| > 1 were identified in each dataset. The intersection of the two gene sets yielded 20 common differentially expressed genes (DEGs), which were further normalized and ranked by significance.

Results: The top ten DEGs identified were NINJ1, PFKFB3, NAMPT1, MAFF, TP53INP2, BBS10, BTG3, GABARA-PL1, METRNL, and CETN3. These genes are known to play direct or indirect roles in immune regulation, inflammation, and metabolic reprogramming in autoimmune contexts. Literature review supported their relevance in immune dysregulation. Furthermore, emerging evidence suggests that MSC-derived exosomes can modulate these pathways, particularly through miRNA delivery and anti-inflammatory protein cargo.

Conclusion: This study highlights ten candidate genes that may serve as potential therapeutic targets for MSC-derived exosome-mediated immune modulation in primary Sjögren's syndrome. These findings offer a promising foundation for future in vitro validation and development of cell-free exosome-based therapies for autoimmune diseases.

Keywords: Primary Sjögren's syndrome, Mesenchymal stem cell, Mesenchymal stem cell-derived exosomes, Transcriptomic analysis, Therapeutic targets

Ps-56: A Patient-Derived 3D Spheroid Model for Cost-Effective Enrichment and Functional Targeting of Ovarian Cancer Stem Cells

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Objective: Epithelial ovarian cancer (EOC) is among the deadliest gynecologic malignancies, primarily due to late-stage diagnosis, intraperitoneal metastasis, and the accumulation of malignant ascites. A key contributor to recurrence and chemoresistance is the presence of ovarian cancer stem cells (OCSCs), whose enrichment remains technically challenging due to their rarity.

Materials and Methods: We developed a simple and cost-effective method using 20% malignant ascitic fluid from high-grade serous ovarian cancer (HGSOC) patients to enrich ovarian cancer stem cells (OCSCs) from both primary tumor-derived cells and OVCAR3 cells. Culturing cells in serum-free media supplemented with ascites under 3D spheroid conditions.

Results: We found significantly enhanced cell viability and the expression of key OCSC markers (CD133, EpCAM, CD44, ALDH1, Oct4, Nanog, Nestin, Sox2). Notably, secondary and tertiary spheroids exhibited a stronger stemness profile and increased resistance to Paclitaxel (PTX) compared to 2D cultures

and primary spheroids. Bioinformatic analysis (TCGA, Enrichr, STRING) highlighted the TGF β /Smad and Hippo/YAP-TAZ pathways as central regulators of OCSC characteristics. Functional assays confirmed that inhibiting YAP (with Verteporfin) or TGF β R1 (with Galunisertib) reduced OCSC marker expression and impaired migration and invasion. Conversely, reactivation of TGF β signaling after YAP inhibition restored stemness features, indicating a critical interplay between TGF β and YAP signaling in maintaining OCSCs.

Conclusion: In summary, our model, which utilizes ascites in 3D culture, provides a physiologically relevant and cost-efficient approach to enrich and study OCSCs. It provides a valuable platform for exploring stemness-associated pathways and testing therapeutic strategies targeting chemoresistant ovarian cancer cells.

Keywords: Ovarian cancer stem cells, Cost-effective enrichment, Hippo-YAP/TAZ signaling, TGF β signaling, Chemoresistance

Ps-57: Producing Conditional NTR Suicide Gene Constructs for Enrichment of NKX6.1 Expressing Pancreatic Endocrine Progenitor Cells

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Objective: Generating functional insulin-secreting β -cells from human embryonic stem cells holds great promise for diabetes therapy. However, differentiation protocols generally lead to heterogeneous populations, containing possible unwanted or undefined cell types, in ways that can affect functionality and safety. The purpose of this study was to develop a genetic system that had the conditional suicide mechanism to specifically enrich for NKX6.1-positive pancreatic endocrine progenitors, by removing non-target cells during differentiation.

Materials and Methods: We constructed both a suicide cassette harboring the NTR gene with flanking LoxP sites under constitutive CMV promoter, and a Cre recombinase gene under the NKX6.1 promoter, which allows selective activation in target progenitor cells, using molecular cloning methods. The constructs were cloned using standard methods of PCR amplification, enzymatic digestion, ligation, and E. Coli transformations. Cloning validation was then performed by colony PCR, restriction analysis, and subsequent Sanger sequencing.

Results: All constructs were cloned and sequence-verified as intended. The system designed permits Cre-mediated excision of the NTR gene in NKX6.1-expressing cells, which makes the NKX6.1+ progenitor population resistant to nitroaromatic prodrugs (such as CB1954). Non-NKX6.1 cells will maintain the NTR gene and will experience drug elimination. This dual-vector system leads to an enrichment of the target progenitor

population and reduces the potential risk for the development of tumorigenesis.

Conclusion: Here we developed a conditional genetic approach in which the Cre-LoxP-mediated excision of the NTR suicide gene specifically enriched for NKX6.1 expressing pancreatic endocrine progenitor cells while allowing for selective ablation of those cells that did not express NKX6.1 using dual constructs. The project revealed the true utility of genetic engineering approaches and a reductionist method to refine cellular composition of populations derived from hESC cells, of which we hope will be important in future developmental biology and stem cell based approaches.

Keywords: pancreatic progenitors, NKX6.1, suicide gene, Cre-LoxP, hESC

Ps-58: Evaluation and Comparison of the Functional Characteristics of CD19 CAR T Cells Produced Under Conventional and Rapid Culture Conditions

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Objective: Chimeric antigen receptor T cell (CAR T) therapy is an innovative treatment modality that has received FDA approval for the management of hematological malignancies. This study aims to compare the functional properties of CAR T cells produced via two different manufacturing protocols: the conventional process (CT-CARaCell19), which takes approximately 12 days, and a fast protocol (FT-CARaCell19), which reduces production time to around 3 days through specific modifications in culture conditions. The primary goal of these modifications is to enhance T cell functionality, including migratory capacity, cytokine production vital for tumor cell eradication, and cytotoxic activity against malignant cells, thereby optimizing overall therapeutic efficacy.

Materials and Methods: CAR T cells from both production methods were derived from three healthy donors. The evaluation focused on several key functional parameters: Migration: Assessed using a transwell migration assay towards chemokine gradients, specifically measuring the chemokine receptor CXCR4 expression and migratory response. Cytotoxicity: Quantified through bioluminescence assays that measure the killing efficiency of CAR T cells against luciferase-expressing tumor cell lines. Degranulation: Analyzed via flow cytometry by measuring CD107a surface expression as an indicator of cytolytic activity. Cytokine Production: Supernatants from co-cultures of CAR T cells with Raji tumor cells were collected to evaluate levels of key inflammatory cytokines such as IFN- γ and IL-2, measured via ELISA.

Results: FT-CARaCell19 cells show higher CXCR4 expression, enhancing their migratory capacity toward target cells. Despite accelerated manufacturing, their cytotoxic activity remains comparable to CT-CARaCell19, indicating preserved effector function. FT-CARaCell19 cells exhibited heightened IFN- γ and IL-2 expression, indicating an amplified inflamma-

tory response that could enhance their anti-tumor efficacy in vivo.

Conclusion: FT-CARaCell19 cells preserve key effector functions while demonstrating enhanced migration, cytotoxic activity and cytokine production compared to conventional cells. Their improved functional profile highlights the potential of rapid manufacturing to produce potent CAR T cell therapies with promising therapeutic benefits.

Keywords: CAR T cell therapy, Migration, Cytotoxicity, Inflammatory cytokine

Ps-59: The Role of Cancer Stem Cells in Tumor Resistance and Relapse: A Therapeutic Challenge

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Objective: Cancer stem cells (CSCs) demonstrate two important properties which make them essential initiators of tumors while allowing their continued growth and eventual re-appearance. The main difficulty in cancer therapy treatment is resistance development mainly because of CSCs which enable quiescent states combined with survival pathway activation and better drug removal capabilities and resistance to programmed cell death and improved DNA damage repair abilities. This research evaluates how to overcome CSCs resistance and use effective combination therapies.

Materials and Methods: The research analysis included database searching in PubMed and Scopus along with Google Scholar from 2018 to 2025 regarding CSCs and their resistance mechanisms with therapeutic intervention studies. Three pioneering research studies achieved selection based on their uniqueness, their detailed mechanistic approach, and their healthcare-related significance.

Results: Activation of the p38 Mitogen-Activated Protein Kinase pathway turns cells into a non-dividing state by switching on the p16-phosphorylated retinoblastoma protein (pRb) axis which creates resistance against chemotherapy. The Hedgehog signaling together with Wnt/ β -catenin system and Notch pathway maintain cancer stem cells and provide them with survival potential. The self-renewal capacity of CSCs diminishes when researchers administer pharmacological inhibitors which include γ -secretase inhibitor CGP049090 as well as tankyrase inhibitors together with Venetoclax and Vismodegib. ATP-binding cassette transporters pull medications from inside cells to the outside leading to decreased drug amounts inside the cells. Clinically, administering multidrug resistance inhibitors with chemo-drugs leads to better drug retention rates. The over expression of B-cell lymphoma 2 (BCL-2) by CSCs enables them to avoid apoptosis but Venetoclax can restore their sensitivity through BCL-2 inhibition. The enzyme Aldehyde dehydrogenase 1 helps defend against oxidative stress and assists in DNA repair processes which makes its inhibition potentially useful for treatment.

Conclusion: The combination of survival pathway inhibitors, efflux pump blockers, and anti-apoptotic agents is recommended for more effective treatment due to CSCs' complex resistance mechanisms.

Keywords: CSCs, Therapeutic Resistance, Tumor Relapse, Therapeutic Intervention, Pathway Inhibitors

Ps-60: Crocin-Based Nanoparticles Mitigate the Activation of the NLRP3 Inflammasome Within Neural Stem Cells

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Objective: One vital carotenoid in saffron, crocin, is known for its significant health advantages. However, despite its therapeutic potential, a few issues hamper its efficacy as a functional agent. These factors encompass insufficient stability, low bio-availability, and limited absorption. Various nanotechnology delivery techniques effectively address these challenges and enhance the efficacy of crocin. Research has underscored the positive impact of crocin on neurodegenerative disorders, attributing it to its anti-inflammatory, antioxidant, and anti-apoptotic characteristics, establishing it as a safe and affordable natural remedy. Crocin can traverse the blood-brain barrier (BBB) and has demonstrated encouraging neuroprotective effects. Recent research has revealed that the release of pro-inflammatory cytokines may trigger a series of events leading to neuronal death, with the inflammasome complex playing a critical role in regulating this process. This research illustrates that Crocin nanoparticles inhibit the NLRP3 inflammasome pathway by reducing reactive oxygen species (ROS) production and mitigating inflammation in neural stem cells.

Materials and Methods: This research utilized SH-SY5Y cells, a human-derived cell line widely used in neuroscience to study neuronal function and differentiation. The study aimed to assess the anti-inflammatory effects of crocin combined with nanoparticles (solid lipid nanoparticles (SLN)-crocin) in in vitro models (SH-SY5Y).

Results: Crocin-SLN was found to inhibit the secretion of interleukin (IL)-1 β and the activity of caspase-1 induced by ROS. These findings indicate that crocin-SLN may attenuate the activation of the NLRP3 inflammasome by preventing the production of mitochondrial reactive oxygen species (mtROS).

Conclusion: The results suggest that crocin-SLN formulations may affect the survival of neural stem cells. Therefore, crocin-SLN could offer therapeutic potential for various inflammatory conditions related to the NLRP3 inflammasome.

Keywords: crocin, nanoparticles (SLN), NLRP3, neural stem cell line (SH-SY5Y)

Ps-61: Chitosan Nanoparticles Containing Curcumin Induce Apoptosis and Cell-Cycle Arrest in MCF7 Cells

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Objective: Breast cancer is the most common cancer among women globally. Early detection and finding effective drugs for resistant forms may enhance treatment and survival. The emphasis shifts to inactive delivery systems for targeted drug delivery to cancer sites. Encapsulating agents in the nanometer range are called nanoparticles (NPs). Depending on their characteristics, sizes, or shapes, they can be divided into several classes. Examples include luminescent nanoporous hybrid materials, metal NPs, fullerenes, and polymeric and ceramic NPs. Interest in natural compounds with potential anticancer properties has grown due to the complexities of tumor biology and the limitations of current therapeutic approaches. One such compound is the bioactive polyphenol curcumin, isolated from *Curcuma longa* L. Turmeric is widely recognized for its numerous biological properties, particularly its anticancer potential. This study investigated the anticancer potential of chitosan NPs-encapsulated curcumin.

Materials and Methods: Following a 24-hour incubation period, curcumin-chitosan NPs were administered to the MCF-7 cells. Apoptosis analysis (using Annexin V/PI), cell-cycle analysis, and real-time PCR were carried out.

Results: The combination treatments of curcumin-chitosan NPs were highly effective in the apoptosis of breast cancer cells (MCF-7) in vitro. Combination therapy with curcumin-chitosan NPs was highly effective in vitro in inducing apoptosis of breast cancer cells (MCF-7). Comprehensive gene expression studies have shown that these anti-cancer effects are related to suppressing the P53, Caspase-3, and P21 genes. This nanoformulation resulted in the cell cycle arrest of the G0 and G1 phase of MCF-7 cells and stimulated the generation of intracellular ROS, which induced apoptosis.

Conclusion: The results suggest that curcumin-chitosan NP formulations may influence the efficacy of apoptosis in breast cancer cells. This feature of chitosan NPs can reduce side effects in healthy cells. In breast cancer treatment, curcumin-chitosan NPs may serve as a biological anti-cancer agent.

Keywords: Curcumin, Chitosan nanoparticles, Apoptosis, Breast cancer cell lines (MCF7)

Ps-62: Molecular Docking Analysis for Antibacterial Activity of LL37 Against Selected Pathogenic Proteins of Staphylococcus Aureus

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Objective: Antibiotic resistance poses a significant challenge to global health, and modifying antimicrobial agents is essential to address this problem. The human cathelicidin LL-37 plays a vital role in the innate immune system, providing defense against bacterial infections. Our previous research findings indicated that the conditioned medium (CM) derived from stem cells from apical papilla exhibited antibacterial properties against *Staphylococcus aureus*, and the presence of the peptide LL-37 was confirmed in this CM. Consequently, we initiated a study to conduct an in silico analysis comparing LL-37 with the conventional antibiotic vancomycin to elucidate the potential mechanisms underlying their antibacterial activities

Materials and Methods: Docking experiments involving

LL37 and vancomycin were carried out against the chosen pathogenic surface proteins of *Staphylococcus aureus*, specifically prostaphopain B (1X9Y), staphopain (1CV8), and MgrA protein (2BV6), utilizing the H-Dock server (<http://hdock.phys.hust.edu.cn/>). A thorough comparative analysis was conducted among these compounds, focusing on free energy and confidence scores, with the results highlighting the top 10 models.

Results: The results were presented in a three-dimensional format, illustrating the effectiveness of the LL37 peptide in binding to three pathogenic surface proteins of *Staphylococcus aureus*, as evidenced by an extensive molecular interaction analysis. The LL37 peptide demonstrated robust interactions with the proteins 1CV8 and 2BV6 across all ten top models, while vancomycin only exhibited valid interactions in models two and six. Furthermore, the LL37 peptide was ultimately found to interact with 1X9Y.

Conclusion: The results of the assay, supported by molecular docking studies, indicate that LL37 serves as an effective inhibitor of pathogenic proteins associated with *Staphylococcus aureus*. Therefore, the insights provided in this research may pave the way for the application of conditioned media derived from stem cells as a novel antimicrobial therapy.

Keywords: LL37, antibacterial activity, *Staphylococcus aureus*, molecular docking

Ps-63: Comparative Effects of Vildagliptin and Exendin-4 on the Differentiation of Insulin-Producing Cells from Adipose-Derived Mesenchymal Stem Cells Cultured in a 3D Nanohydrogel Scaffold

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Objective: This study aims to compare the effects of Vildagliptin (VG) and Exendin-4 (EX-4) on the differentiation of adipose-derived mesenchymal stem cells (AD-MSCs) into insulin-producing cells (IPCs) within a 3D nanohydrogel scaffold, with the goal of developing a regenerative therapy for diabetes. The 3D scaffold's biomimetic properties and controlled drug release are hypothesized to enhance IPC differentiation and function under diabetic conditions, addressing the need for effective β -cell replacement strategies.

Materials and Methods: AD-MSCs were cultured in a 3D nanohydrogel scaffold composed of hyaluronic acid, gelatin, and collagen IV (pore size: 50–100 nm, stiffness: 1–2 kPa) and treated with VG or EX-4 under diabetic conditions (3D-DM). Gene expression of PDX1, GLUT2, and Insulin was analyzed via qRT-PCR, normalized to GAPDH. Cell viability, morphology, and glucose-stimulated insulin secretion (GSIS) were assessed using MTT assays, microscopy, and ELISA, respectively.

Results: The 3D-DM+EX-4 group exhibited the highest gene expression, with PDX1 ($p < 0.01$), GLUT2 ($p < 0.01$), and Insulin ($p < 0.05$) surpassing 3D-DM+VG, PDX1 ($p < 0.001$) and 3D-DM groups. EX-4 enhanced differentiation via cAMP/PKA and MAPK/ERK pathways, while VG excelled in GSIS (at 25 mmol/L glucose, $p < 0.001$) through PI3K/Akt signaling. In diabetic conditions, VG and EX-4 restored insulin secretion ($p < 0.01$) compared to 3D-DM.

Conclusion: The nanohydrogel scaffold enhanced VG and EX-4-mediated IPC differentiation, with EX-4 favoring type 1 diabetes (β -cell replacement) and VG benefiting type 2 diabetes (glycemic control). Future in vivo studies are needed to validate

this approach for clinical translation.

Keywords: Vildagliptin, Exendin-4, Adipose-derived mesenchymal stem cells, Type 1 diabetes, β -cell replacement

Ps-64: Potentiation of MSC Immunomodulation through Nanos2: In Vitro and In Vivo Evidence

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Objective: Mesenchymal stromal/stem cells (MSCs) modulate the mammalian immune system, and their therapeutic potency can be enhanced by regulating key proteins. Nanos2, an RNA binding protein involved in spermatogonial signaling pathways, downregulates numerous immune-related genes in mouse embryonic fibroblasts. We hypothesized that Nanos2 acts as a potent immunosuppressive factor. This study measured immune gene expression profiles in mouse MSCs (mMSCs) and assessed their function after ectopic Nanos2 expression.

Materials and Methods: Interferon (IFN γ) and poly(I:C) served as inflammatory stimuli to elicit an immune response. We then compared how control mMSCs and Nanos2-overexpressing mMSCs interacted with mouse peripheral blood mononuclear cells (mPBMCs). To evaluate their resilience in an inflammatory environment, both cell types were exposed to conditioned medium rich in pro inflammatory cytokines. We examined their functional behavior, against tumor cells and immune cells, using both in vitro assays and in vivo models. Finally, LPS induced lung inflammation model was treated with the injection of both control mMSCs or Nanos2 overexpressing mMSCs.

Results: Nanos2 overexpression significantly downregulated (>2 fold, $p<0.01$) genes controlling inflammatory response, cell-cell adhesion, and wound healing. Nanos2 mMSCs inhibited mPBMC proliferation by up to 60% after IFN γ /poly(I:C) pretreatment ($p<0.001$). Consistent with prior data, Nanos2 mMSCs enhanced B16 F0 tumor growth, whereas control MSCs yielded minimal or no tumor development. Inflammation assessment of the LPS induced lung inflammation indicated lower histopathology score in Nanos2 MSC group.

Conclusion: Nanos2 overexpression equips MSCs with robust anti inflammatory properties, maintained even in pro inflammatory environment. Nanos2 engineered MSCs may represent a promising strategy to control acute lung inflammation. Further studies on safety and dose response are required for clinical application.

Keywords: Mesenchymal Stromal/Stem Cells, Immunomodulatory, Nanos2

Ps-65: Molecular Drivers of Carcinogenesis in Thyroid Malignancies: The Role of BRAF V600E and TERT Promoter

Mutations

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Objective: Thyroid cancer represents the most prevalent endocrine malignancy, with papillary thyroid carcinoma (PTC) comprising the majority of cases. In recent years, accumulating molecular evidence has elucidated the significance of genetic and epigenetic alterations in thyroid tumorigenesis. Chief among these are the BRAF V600E mutation and TERT promoter mutations, both of which are implicated in enhanced tumor proliferation, aggressiveness, and resistance to standard therapies.

Materials and Methods: A systematic review of peer-reviewed articles from 2018 to 2024 was performed across PubMed, Scopus, and Web of Science. Studies were selected based on their focus on the molecular mechanisms and clinical significance of BRAF and TERT alterations in thyroid cancer. Special attention was given to pathway interactions—particularly MAPK/ERK signaling—co-mutation patterns, noncoding RNAs, and epigenetic regulation.

Results: The BRAF V600E mutation, present in approximately 40–60% of PTC cases, results in constitutive activation of the MAPK pathway, driving cellular proliferation and dedifferentiation. TERT promoter mutations, though less frequent, are strongly associated with increased recurrence, metastasis, and mortality. Co-occurrence of BRAF and TERT mutations leads to a synergistic oncogenic effect, markedly enhancing tumor aggressiveness. Additional molecular interactions with long noncoding RNAs (lncRNAs) and DNA methylation patterns contribute further to disease complexity and progression.

Conclusion: A detailed understanding of the molecular underpinnings of thyroid carcinogenesis is vital for risk stratification and personalized treatment. BRAF V600E and TERT promoter mutations not only serve as prognostic biomarkers but also hold promise as targets for molecular therapies. Their clinical integration could significantly advance precision oncology in thyroid cancer management.

Keywords: BRAF V600E, TERT promoter, thyroid cancer, carcinogenesis, molecular biomarkers

Ps-66: Lung Organoids as a Novel Platform for Drug Screening in Personalized Medicine

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Objective: Considering the high rates of prevalence and mortality associated with respiratory diseases, there is a strong demand for innovative diagnostic and therapeutic approaches. Lung organoids, derived from induced pluripotent stem cells (iPSCs) or lung progenitor cells, serve as a diagnostic tool that can mimic the characteristics of human lung tissue in vitro. These three-dimensional structures offer a physiologically relevant micro-environment for disease modeling and drug screening. These models can assess patient-specific drug responses, particularly in different respiratory disorders, including pulmonary diseases such as cystic fibrosis, idiopathic pulmonary fibrosis, and viral infections. Lung organoids can provide a powerful tool for

identifying the best therapeutic approach for each patient.

Materials and Methods: Lung organoids are generated by incorporating of specific growth factors into a three-dimensional matrix, guiding the differentiation of stem cells into alveolar and bronchial lineages. For morphological characterization of organoids, confocal microscopy can be used, whereas immunostaining can be utilized to verify cellular composition. After the formation of lung organoids, drug screening assays are conducted to assess cytotoxicity, therapeutic efficacy, and pharmacokinetics in a patient-specific manner. Finally, to evaluate treatment-induced molecular changes, gene expression analysis via RNA sequencing can be employed.

Results: Lung organoids are effective tools that can successfully replicate the key features of lung tissue, including airway architecture and surfactant production. Drug screening assays revealed differential responses that correlate with patient-specific genetic and molecular profiles. Their ability to model disease progression in a controlled microenvironment highlights their potential to optimize personalized therapeutic approaches.

Conclusion: In summary, lung organoids offer novel platform for disease modeling and drug screening, facilitating targeted personalized treatment strategies for respiratory disorders. Their ability to recapitulate patient-specific responses can minimize the reliance on trial-and-error medication strategies and ultimately improves clinical outcomes.

Keywords: Lung Organoids, Personalized Medicine, Drug Screening, Disease Modeling

Ps-67: Three-Dimensional Co-Culture Condition for U266 Myeloma Cells

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Objective: Multiple myeloma (MM), accounts for 2% of all cancers and 10% of hematologic malignancies and despite development of novel therapies remains an incurable disease. MM bone marrow (BM) microenvironment composed of different cellular elements and extra-cellular matrix molecules that together supports tumor progression and treatment resistance. Conventional models targets three-dimensional (3D) interactions of myeloma cells and other BM microenvironment compartments, however mostly rely on patient samples and artificial substances that naturally not found in BM microenvironment. Thus, we developed a simple, cost-effective and patient-free model of U266 cells for drug-screening studies and further exploring disease biology.

Materials and Methods: Plasma blood from three healthy donors was used to generate fibrin gels. Moreover, different factors affecting formation and stability of fibrin gels were assessed. U266 cells with bone marrow-mesenchymal stem cells (BM-MSCs) and human umbilical vein endothelial cells (HUVECs) were cultured under different matrix-based and gel-free conditions. Furthermore, proliferation and survival rates of U266 cells were evaluated and compared.

Results: Optimal calcium chloride and tranexamic acid concentrations were 1 mg/ml and 5 mg/ml for fibrin-gel formation and stability. U266 cells showed increased proliferation and viability in 3D mono-cultures. However, U266 cells formed

3D-structures in gel-free co-culture condition, with proliferation and survival rates significantly higher compared to other fibrin-based conditions.

Conclusion: Therefore, 3D co-culture of U266 cells along with BM-MSCs and HUVECs in gel-free condition resulted in significantly increased expansion and viability rates of myeloma cells and our 3D model could be a simple and available tool for future drug-screening studies.

Keywords: multiple myeloma, co-culture, three-dimensional cell culture, fibrin-gel, proliferation

Ps-68: Curcumin-Based Strategies Targeting Breast Cancer Stem Cells: From Derivatives to Combination Therapies

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Objective: Breast cancer stem cells (CSCs) are a subpopulation that cause tumor growth, metastasis, and recurrence due to their self-renewal and resistance to conventional therapy. Curcumin, a natural polyphenol, possesses pleiotropic activities by modulating multiple signal transduction pathways relevant to CSC biology. These characteristics make curcumin a promising drug candidate for developing multifaceted therapeutic modalities against CSCs.

Materials and Methods: A systematic literature search was performed in the PubMed database on May 2, 2025, utilizing Boolean operators with keywords such as “Curcumin,” “Breast Cancer,” and “Cancer Stem Cells.” The initial search yielded 52 articles. One inclusion criterion was established: studies that investigated curcumin-based combination therapies, drug delivery systems, or curcumin-derived/analog compounds. Following this screening process, 33 articles qualified and were included for detailed review analysis.

Results: Studies have identified three main curcumin-based strategies targeting CSCs of the breast. Combination therapies with other drugs such as piperine, salinomycin, quinacrine, and other chemotherapeutic or targeted drugs exert synergistic effects, enhancing the cytotoxicity of curcumin and reducing CSC-associated stemness. Drug delivery systems such as niosomes, micelles, and nanoparticles have been developed to bypass curcumin's poor bioavailability, enabling more efficient and targeted delivery to CSC-enriched tumor sites. In addition, synthetic analogs and derivatives of curcumin, like C1, AzCDF, Comp34, and others, demonstrate improved stability, activity, and pharmacokinetics. Collectively, these strategies underline the potential of curcumin as a multi-targeted compound in CSC-based breast cancer therapies.

Conclusion: This systematic review emphasizes that curcumin-based approaches constitute a versatile strategy for targeting breast CSCs. The findings illuminate the potential of multifaceted interventions, including combination therapies, modern delivery systems, and structure-modified analogs, to address CSC-mediated resistance mechanisms. These insights carry significant implications for cancer biology research and support the further development of targeted therapies aimed at eradicating CSCs and enhancing breast cancer treatment outcomes.

Keywords: Curcumin, Breast Cancer Stem Cells, Combination Therapy, Drug Delivery Systems, Curcumin Derivatives

Ps-69: The Role of miR-182 in Prostate Cancer Progression:

A Key Biomarker Driving Oncogenic Signaling Pathways

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Objective: Prostate cancer (PCa) is a major cause of cancer morbidity and mortality in men worldwide. Among the various molecular regulators involved in its pathogenesis, microRNAs (miRNAs) are identified as prime post-transcriptional regulators of gene expression. Notably, miR-182 has been recognized as a significant contributor to prostate tumorigenesis. This review focuses on the pivotal role played by miR-182 in the oncogenic pathways of prostate cancer development.

Materials and Methods: A systematic literature search was conducted in the PubMed database (title/abstract fields) on April 20, 2025. Boolean search operators were employed with keywords such as “miR-182” and “prostate cancer.” The search yielded 51 articles. Eligibility criteria were applied in two distinct stages: (1) studies investigating the involvement of miR-182 in oncogenic signaling pathways, excluding drug-treatment research, were selected (n=15); (2) studies assessing miR-182 as a biomarker were subsequently included (n=6). A total of 21 studies met the inclusion criteria and were retained for detailed analysis.

Results: Studies have shown that miR-182 is significantly overexpressed in prostate cancer tissues and cell lines, and this upregulation correlates with Gleason Pattern, advanced tumor stage, and aggressive tumor characteristics. Functionally, based on original research and gene expression profiling data, miR-182 downregulates several prominent tumor suppressor genes that are involved in remarkable oncogenic pathways such as Phosphatidylinositol 3-kinase/Protein Kinase B (PI3K/Akt), Wnt/ β -catenin, Hypoxia-Inducible Factor 1- α (HIF-1 α), and other related pathways. Moreover, while most studies suggest that miR-182 promotes Epithelial-Mesenchymal Transition (EMT), few studies propose that it may also inhibit EMT, indicating a potential dual role depending on the context of this process.

Conclusion: These pathways function as critical drivers of tumor progression and their aggressive phenotype, leading to adverse clinical outcomes in prostate cancer patients. The consistent association of miR-182 expression with prostate cancer pathological features indicates its potential as a molecular biomarker for disease stratification and prognosis.

Keywords: miR-182, Prostate Cancer, Oncogenic Signaling, Biomarker

Ps-70: Protective Effect of Human Placental Extract Against H₂O₂ Induced Oxidative Damage in Human Dermal Fibroblasts

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Objective: One key strategy for preventing skin aging involves safeguarding fibroblast cells from oxidative stress. Extensive research has already explored the beneficial impact of human placenta extract (HPE) on wound healing, including re-epithelialization, synthesis of extracellular matrix (ECM) proteins

particularly collagen and elastin, cell proliferation, and migration. In this experimental study, the focus was on assessing HPE's antioxidant properties in countering hydrogen peroxide (H₂O₂)-induced damage model to human dermal fibroblasts (HDFs).

Materials and Methods: To create the aging model, HDFs were exposed to varying concentrations of hydrogen peroxide (H₂O₂) for a 2-hour duration. The optimal dose was determined using the MTS test and Trypan Blue staining. The dose assessment of the human placental extract was also performed using Trypan Blue staining. To establish the ageing model, human skin fibroblasts were exposed to 400 μ M H₂O₂ for 2 h. HDFs were treated with 50 μ g/ml HPE for 24h before or/and after H₂O₂ exposure. A total of 72 h following the H₂O₂ treatment, we measured senescence-associated β -galactosidase (SA- β -Gal), cellular ROS, catalase, hydroxyproline, TGF- β 1, VIM and pro-inflammatory cytokine (IL-6) levels, as well as the expression of senescence-associated genes (P53 and P21).

Results: The obtained results indicated that under oxidative stress, HPE significantly reversed the SA- β -Gal levels induced by H₂O₂. Additionally, both pre- and post-treatment regimen by HPE down-regulated the expression of senescence marker genes. Moreover, HPE declined oxidative stress biomarkers such as catalase and cellular ROS.

Conclusion: The findings suggest that HPE holds promise as a natural-based cosmeceutical agent for delaying and managing skin aging.

Keywords: Human Dermal Fibroblast cells, Human Placenta Extract, H₂O₂, Anti-aging

Ps-71: Targeted Nanodelivery of Dexamethasone via MSC-derived Exosomes for Pulmonary Protection in Septic Mice

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Objective: The use of biological nanocarriers such as mesenchymal stem cell-derived exosomes (MSC-Exos) offers a promising strategy for targeted drug delivery with enhanced therapeutic efficiency and reduced systemic toxicity.

Materials and Methods: In this study, we evaluated the potential of exosomes loaded with dexamethasone (Dex-Exos) to mitigate sepsis-induced lung injury via targeted nanodelivery of anti-inflammatory agents. A cecal ligation and puncture (CLP) model was used to induce sepsis in C57BL/6 mice. Experimental groups included sham, CLP, CLP + free Dex, CLP + MSC-Exos, and CLP + Dex-Exos. Lung tissues and bronchoalveolar lavage (BAL) fluids were collected 24 hours post-treatment for histological and biochemical analysis.

Results: Mice treated with Dex-Exos showed a marked reduction in immune cell infiltration, alveolar wall thickening, and

vascular congestion compared to the untreated CLP group. Additionally, total protein and leukocyte levels in BAL fluid were significantly decreased. Notably, Dex-Exos exerted similar or superior therapeutic effects compared to free Dex despite carrying significantly lower drug concentrations, highlighting the efficiency of exosome-mediated targeted delivery.

Conclusion: This study underscores the potential of MSC-derived exosomes as natural, biocompatible nanocarriers for targeted corticosteroid delivery in inflammatory lung disorders, paving the way for safer and more precise anti-inflammatory therapies.

Keywords: Nanodelivery, Mesenchymal stem cell, exosomes, Sepsis, dexamethasone

Ps-72: Neurovascular Protection of Melatonin-Pretreated Astrocyte-Derived Extracellular Vesicle in Ischemic Stroke in mPFC

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Objective: Ischemic stroke (IS) induces profound neurovascular damage characterized by neuronal loss, endothelial dysfunction, and disruption of the blood-brain barrier. Extracellular vesicles (EVs) derived from astrocytes have emerged as promising therapeutic agents due to their ability to deliver protective molecular cargo. However, strategies to enhance their reparative potential are needed. Melatonin, a neuroprotective agent with antioxidant and anti-inflammatory properties, has been shown to modulate the bioactivity of donor cells and their secreted EVs. In this study, we investigated the therapeutic efficacy of melatonin-pretreated astrocyte-derived extracellular vesicle (MT-EV) in a mouse model of IS.

Materials and Methods: Male mice were subjected to photothrombotic IS, and after 5 days, astrocyte EV (AS) and MT-EV were locally injected into the penumbra of the lesion site in the medial prefrontal cortex. After 21 days, histological analysis was performed, and neuronal morphology and infarct regions were evaluated across groups. EV uptake and neural stem cell interactions were assessed via DiI and Nestin staining, and vascular integrity was quantified using von Willebrand Factor (vWF) immunolabeling.

Results: DiI-labeled EVs were detected within peri-infarct regions, colocalizing with Nestin-positive neural stem cells. This indicates the successful delivery of EVs to neurogenic niches and suggests the potential for modulating endogenous regeneration mechanisms. Control animals exhibited severe ischemic damage, including pyknotic nuclei, tissue vacuolization, and necrosis. AS-EV-treated brains showed partial restoration of cortical morphology, while MT-EV treatment further preserved tissue integrity with reduced necrotic zones. Sham-operated animals demonstrated a significant reduction in vWF expression, consistent with vascular disruption post-stroke. Both AS-EV and MT-EV treatments restored vWF-positive vascular structures.

Conclusion: This study provides foundational evidence for the use of MT-EVs as an optimized therapeutic strategy in IS and

underscores the promise of cell-free, EV-based therapies for CNS injury.

Keywords: Extracellular vesicle, ischemic stroke, astrocytes, melatonin

Ps-73: Protective Effects of Plant-Derived Antioxidants Against Di(2-ethylhexyl) Phthalate-Induced Oxidative Stress in Rat Bone Marrow Mesenchymal Stem Cells: Preserving Viability and Proliferation

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Objective: Di(2-ethylhexyl) phthalate (DEHP) is used in the production of various polyvinyl chloride products in medicine. This chemical compound is released from these products and induces oxidative stress in bone marrow mesenchymal stem cells (BMSCs) in rats. In the present study, various plant-derived antioxidants were utilized to counteract DEHP-induced toxicity.

Materials and Methods: BMSCs extracted from Wistar rats at passage three were cultured under the influence of various antioxidant concentrations for four days. Based on the absence of cytotoxicity and increased cell proliferation, concentrations of 0.25 μ M gallic acid (GA), 0.25 μ M catechin (CH), and 0.1 μ M curcumin (Cur) were selected to counteract the toxicity induced by 100 and 500 μ M DEHP. These concentrations were used to assess cell viability, proliferation (PDN), and oxidative stress mitigation.

Results: Higher concentrations than 0.25 μ M of GA and CH and 0.1 μ M of Cur reduced cell viability and proliferation, whereas the aforementioned concentrations enhanced BMSC proliferation. GA demonstrated the best performance compared to CH and Cur, completely neutralizing the toxic effects of 100 μ M DEHP. However, none of the antioxidants could fully counteract the toxicity of 500 μ M DEHP. In oxidative stress analysis, GA showed the most significant reduction in malondialdehyde levels, with the highest improvement in catalase and superoxide dismutase enzyme activity observed in the GA + 100 μ M DEHP treatment group. This suggests that GA possesses superior antioxidant properties, as reflected in its measured antioxidant activity.

Conclusion: It can be said that the best antioxidant for counteracting the toxic effects of DEHP is GA. Therefore, it is recommended to consume plant-based products rich in GA, such as black tea and dried fruits, on a daily basis.

Keywords: viability, DEHP, rat bone marrow mesenchymal stem cells, antioxidant, oxidative stress

Ps-74: Synergistic Effects of Zinc Oxide Nanoparticles and Lactococcus lactis Lysate on Cytotoxicity and Apoptosis in MCF-7 Cells

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Objective: Breast cancer remains a leading cause of mortality among women, prompting the development of novel therapeutics. Nanoparticle-based agents and probiotic derivatives have

emerged as promising candidates. This study evaluates the synergistic cytotoxic and apoptotic effects of zinc oxide (ZnO) nanoparticles and *Lactococcus lactis* lysate in MCF-7 breast cancer cells.

Materials and Methods: *Lactococcus lactis* (NCTC 6681) was cultured in MRS broth, and its lysate was prepared by repeated freeze-thaw cycles. MCF-7 cells were treated with ZnO nanoparticles (3.125–1600 µg/mL), *L. lactis* lysate, the combination of ZnO nanoparticles and *L. lactis* lysate, and tamoxifen as a positive control. Cytotoxicity was assessed via MTT assay at 24, 48, and 72 hours. Expression levels of bax, bcl2, p21, casp9, and cdk4 were measured by Real-Time PCR, using GAPDH as the reference gene.

Results: IC50 values at 24 hours for ZnO, *L. lactis* lysate, combination of ZnO and *L. lactis* lysate, and tamoxifen were 49.68 µg/mL, 61.53 µg/mL, 31.05 µg/mL, and 11.68 µg/mL respectively while at 48 and 72 hours, the combination showed enhanced cytotoxicity at IC50 = 26.38 and 24.79 µg/mL. Gene expression analysis revealed that the combination treatment significantly upregulated pro-apoptotic markers BAX (1.723-fold), CASP9 (1.75321-fold), and P21 (1.72914-fold), while downregulating the anti-apoptotic BCL2 (0.55287-fold) and cell cycle promoter CDK4 (0.544-fold). These effects closely paralleled those of tamoxifen, which induced comparable changes. (BAX: 1.8066-fold; CASP9: 1.82977-fold; P21: 1.79419-fold; BCL2: 0.50991-fold; CDK4: 0.49655-fold).

Conclusion: Co-treatment with ZnO nanoparticles and *L. lactis* lysate exerts a synergistic pro-apoptotic effect on MCF-7 cells. These findings support their potential as an adjunct therapeutic strategy in breast cancer management.

Keywords: Apoptosis, Cell Cycle, *Lactococcus lactis* lysate, MCF-7 cells, Zinc Oxide Nanoparticles

Ps-75: Two-layered Electrospun Nanofibrous Mat Loaded Chitosan Nanoparticles, Growth Factors and Hair Follicle Bulge Stem Cells Can Promote Wound Healing in Rat

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Objective: Wound healing remains a demanding medical problem despite significant advances in regenerative medicine. Mesenchymal, hair follicle and pluripotent stem cells are candidate populations for therapeutically relevant applications. Hair follicle bulge stem cells with scaffolds and growth factors can promote the healing of wounds.

Materials and Methods: In this study, electrospun polycaprolactone/silver sulfadiazine (PCL/SSD), polycaprolactone/collagen (PCL/COLL) was designed as two-layered nanofibrous mats. Chitosan nanoparticles containing EGF and bFGF growth factors prepared by ionic gelation process were added to the two-layered nanofibrous mats. The EGF and bFGF release were assayed. Immunocytochemistry and flow cytometry were performed on the bulge stem cells. The tracked cells were seeded on the nanofibrous mat and transplanted onto the rat skin. H&E and Masson's trichrome were used to study tissue remodeling and collagen synthesis.

Results: The results showed that the nanofibrous composite

was optimized for attaching and spreading bulge stem cells. In vivo assessment showed complete skin repair in the two-layered nanofiber mat containing bulge stem cells and growth factor-containing nanoparticles group on day 14 post-wounding.

Conclusion: The two-layered nanofiber mat with bulge stem cells and nanoparticles containing growth factors could suggest as a suitable wound dressing of nanofiber membranes to reduce the healing time.

Keywords: hair follicle stem cells, nanofiber, wound healing, growth factor

Ps-76: Siponimod Delivery with FA-PEG-PCL/mPEG-PCL Nanoparticles

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Objective: Multiple sclerosis (MS) is a chronic autoimmune disorder of the central nervous system, with limited treatment options for its progressive forms. Siponimod, a selective sphingosine 1 phosphate receptor, has shown promise in managing MS symptoms, particularly in secondary progressive MS. However, systemic side effects and suboptimal delivery to inflamed neural tissues remain challenges. Nanoparticle-based drug delivery systems, such as folic acid-conjugated poly (ethylene glycol)/ methoxy poly (ethylene glycol)-poly(ε-caprolactone) (FA-PEG-PCL/mPEG-PCL), offer a promising strategy for brain-targeted therapy by enhancing BBB penetration, improving bioavailability, and enabling controlled release of the drug. Despite the therapeutic potential, studies exploring nanocarrier-based delivery systems in MS models remain limited; therefore, this study aimed to develop and evaluate a folate-modified nanoparticle formulation for targeted delivery of siponimod in an EAE mouse model

Materials and Methods: In this study Siponimod-loaded FA-PEG-PCL/mPEG-PCL nanoparticles (Sipo@NPs) were prepared via the dialysis method. The physicochemical characteristics of the nanoparticles were assessed using dynamic light scattering (DLS). Drug loading and release studies were conducted using dialysis assays. Release profiles were evaluated under two pH conditions (5.5 and 7.4) to mimic the intracellular and physiological environments, respectively.

Results: DLS analysis revealed a mean particle size of 176.52 nm for Sipo@NPs, indicating favorable size distribution for brain targeting [1]. Drug release studies showed a pH-responsive profile, with a faster release of siponimod at pH 5.5 compared to pH 7.4, suggesting enhanced release in acidic environments such as inflamed tissues. The formulation remained stable for over 72 hours in both conditions, demonstrating its potential for sustained drug release [2].

Conclusion: A novel micellar drug delivery system was developed, which was composed of Siponimod (as the model drug), folate (as the targeting ligand), and PEG-PCL/mPEG-PCL (as the self-assembling material) with a desirable nanoscale size and exhibited controlled, pH-dependent release behavior. These

properties, along with the folic acid ligand on the surface of the nanoparticles, suggest that the formulation may enhance targeted delivery in inflammatory conditions such as those modeled by EAE.

Keywords: Siponimod, Nanoparticles, Drug Delivery, Sustained release, Multiple Sclerosis

Ps-77: Developing a High-Throughput Spheroid Culture System for Monitoring Colorectal Cancer Cell Activity

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Objective: Colorectal cancers with high rates of mortality are devastating pathological conditions in both developing and industrialized societies. Therefore, designing and developing accurate 3D culture systems to recapitulate in vivo-like conditions is highly recommended for investigating the efficiency of therapeutic strategies. Most of the previously introduced 3D culture systems are not suitable to mimic the relatively in vivo niche in laboratory settings; if so, the suggested models, such as spheroid or tumoroid systems, lack enough structural integrity and cellular interactions for prolonged culture times.

Materials and Methods: Here, we aimed to fabricate an in vitro 3D colorectal spheroid model with appropriate structural integrity and cellular interactions for a long-term culture system using a hydrogel-based hanging drop method. To this end, human adenocarcinoma colorectal HT-29 cells were incorporated inside a biomimetic microenvironment composed of natural and synthetic polymers. Physicochemical properties and hydrogel intermolecular interactions were evaluated using FTIR, XRD, Raman, NMR, dot mapping, EDS, and FESEM spectroscopy. The stability, survival rate, and existence of a centric hypoxic area were monitored using different biological analyses, such as MTT and other analyses, over nine weeks.

Results: Data indicate that the optimum hydrogel structure composed of modified Methylcellulose with hybrid polymers yielded suitable structural integrity and cell-to-cell interactions in which the size of spheroids became less over 3 days. Bright-field images revealed the increase in spheroid compaction after 6 days.

Conclusion: Taken together, the present data indicated the eligibility of developed hydrogel in the induction and maintenance of colorectal HT-29 cells spheroids over time, comparable to in vivo-like conditions.

Keywords: Cancer, 3D culture, hanging drops, hydrogel

Ps-78: Modeling Tumor and Molecular Characteristic of HT-29 Spheroids: Quantitative PCR Profiling of VEGF and Hypoxia-Responsive Genes

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Objective: Three-dimensional (3D) spheroid cell culture has

attracted considerable attention to better mimic cell-to-cell and cell-to-extracellular matrix (ECM) interactions that occur in vivo. These parallels offer a viable platform for drug screening and treatment efficacy assessment, as well as significant promise for researching the biological characteristics of malignancies. In this research, modified methylcellulose combined with a hybrid polymer offers its advantages and superior 3D culture systems using the hanging drops method.

Materials and Methods: In this research, human adenocarcinoma colorectal HT-29 cells cultured using hanging drop method and the formation and compaction of spheroids created using natural and synthetic hydrogels were assessed over time to simulate hypoxic tumor cores. Molecular studies were performed on spheroids on the fifth day of spheroid formation. To evaluate hypoxia-induced molecular responses, quantitative PCR (qPCR) was performed to assess the expression of hypoxia-related genes, including HIF-1 α , along with VEGF-A, a key regulator of angiogenesis.

Results: HT-29 spheroids demonstrated a significant upregulation of HIF-1 α and VEGF-A when compared to 2D monolayer cultures, suggesting the presence of a hypoxic core and an angiogenic switch commonly found in solid tumors. These results validate the hypoxic character of the 3D spheroids and underscore the role of hypoxia in promoting pro-angiogenic signaling in colorectal cancer.

Conclusion: The results indicate that HT-29 spheroids serve as a reliable in vitro model for investigating tumor hypoxia and VEGF-mediated pathways associated with cancer progression and therapeutic resistance.

Keywords: Human Colorectal cancer spheroids, Hypoxia, angiogenesis, Hanging drop

Ps-79: Enoxacin Inhibits the Proliferation, Migration, and In Vivo Tumorigenesis of Embryonal Carcinoma Cells

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Objective: Cancer continues to be a leading cause of death globally. Tumors consist of a subgroup of cells called cancer stem cells (CSCs), which enhance tumor progression and recurrence. Notably, the NTERA-2 (NT-2) cancer stem-like pluripotent cell line serves as a relevant model for studying potential therapies. The small molecule enoxacin is an RNA interference (RNAi) enhancer, increasing the maturation rate of various cellular miRNAs. In the present study, the anti-cancer effect of enoxacin was evaluated in the human embryonal carcinoma cell line NT-2.

Materials and Methods: NTERA-2 cells were treated with 124 μ M enoxacin, and its effects on cell viability, proliferation, and migration were assessed. Cell cycle profiling and apoptosis were analyzed via flow cytometry, while clonogenic and migration assays were done to evaluate invasive potential of the cells. Gene and miRNA expression were examined to elucidate mechanistic pathways. The inhibitory effects of enoxacin on tumorigenesis were analyzed in a Nude mouse model. Data (3 replicates; mean $\pm$ SD) were analyzed using GraphPad Prism 8 software.

Results: Our findings show that enoxacin dramatically slows the growth of NT-2 cells. It triggers cell cycle arrest and pro-

motes apoptosis, ultimately reducing both the number and viability of these cells. Additionally, enoxacin weakens the cells' ability to migrate and form colonies. Importantly, our in vivo experiments reinforce these results, demonstrating that enoxacin effectively suppresses tumor formation in Nude mice, further highlighting its potential as a promising therapy against malignant carcinomas.

Conclusion: This study demonstrates that enoxacin effectively suppresses NT-2, impairing their proliferation, migration, and tumorigenic capacity.

Keywords: NTERA-2, Enoxacin, Cancer stem cells, miRNA, RNAi

Ps-80: Evaluation of Annona squamosa/ZnO Nanocomposite on Tissue Integrity and Biochemical Markers in Male Mice with Induced Cancer

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Objective: Annona squamosa L. (custard apple) seed extract contains bioactive acetogenins with known anticancer potential. Zinc oxide nanoparticles (ZnO NPs) demonstrate selective cytotoxicity toward tumor cells via reactive oxygen species generation. This study evaluated a green-synthesized A. squamosa/ZnO nanocomposite for its effects on hematological, biochemical, and histopathological parameters in a male mouse cancer model.

Materials and Methods: In this study, a nanocomposite was synthesized by combining methanolic extract of A. squamosa seeds with zinc nitrate, and its properties were confirmed using UV-Vis spectroscopy, FESEM, AFM, EDS, XRD, and FTIR. One hundred male Swiss albino mice (8–12 weeks old) received weekly intraperitoneal injections for two months. Five groups were induced with cancer, of which four were co-treated with different doses of the nanocomposite (40, 80, 120, 200 mg/kg), and one served as a cancer control. The remaining five groups received the same nanocomposite doses without carcinogen. At the end of the study, blood samples were collected for complete blood count, liver enzymes, kidney markers, total protein, and electrolyte analysis. Liver and kidney tissues were examined histologically for pathological evaluation.

Results: Cancer-only mice exhibited significant weight loss and elevated liver enzymes and renal markers versus healthy controls. In contrast, nanocomposite-treated mice demonstrated dose-dependent maintenance of body weight, normalization of liver enzyme activity and renal function parameters, and increased total protein levels. Electrolyte analysis revealed significant modulation of potassium and chloride concentrations, whereas sodium and calcium remained unchanged. Histopathological evaluation showed marked attenuation of hepatic necrosis, inflammatory infiltration, and renal tubular degeneration in treated mice compared to the cancer control.

Conclusion: These findings indicate that A. squamosa/ZnO nanocomposite confers protective and corrective effects on liver and kidney function in a murine cancer model and support further investigation into its potential as a safe adjunct in anticancer therapy.

Keywords: A. squamosa, Cancer, kidney function, liver enzymes, ZnO Nanocomposite

Ps-81: Comparative Analysis of Plant-Derived Antioxidants in Enhancing Osteogenic Differentiation of Rat Bone Marrow Mesenchymal Stem Cells Exposed to Di(2-ethylhexyl) Phthalate

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Objective: Given the use of di(2-ethylhexyl) phthalate (DEHP) as a plasticizer in polyvinyl chloride products and its oxidative stress effects, the potential toxicity of bone marrow mesenchymal stem cells (BMSCs) and, consequently, the development of osteoporosis due to impaired differentiation into osteoblasts is not unexpected. In this study, the effects of three plant-derived antioxidants in counteracting lipid peroxidation were examined. **Materials and Methods:** BMSCs were extracted from Wistar rats at passage three and cultured in an osteogenic environment under various concentrations of antioxidants for 21 days. Given the absence of cytotoxic effects and the observed increase in cell proliferation, concentrations of 0.25 µM gallic acid (GA) and catechin (CH), as well as 0.1 µM curcumin (Cur), were used to counteract the effects of 100 µM di(2-ethylhexyl) phthalate (DEHP). Subsequently, matrix production in osteoblast cells and the induction of oxidative stress were evaluated.

Results: Statistical analysis revealed that concentrations exceeding 0.25 µM and 0.1 µM of these antioxidants resulted in reduced cell viability. Additionally, it was observed that these concentrations compensated for the decline in viability of DEHP-treated cells compared to the control group, although Cur exhibited a lower protective effect in comparison to GA and CH. Furthermore, the toxic effects of DEHP on matrix production were fully mitigated by these antioxidants, as confirmed by Alizarin staining, calcium concentration measurement, and alkaline phosphatase activity analysis. Oxidative stress analysis demonstrated that GA and CH were capable of completely counteracting the effects of DEHP, whereas Cur exhibited a weaker protective effect due to its hydrophobic properties.

Conclusion: Based on the present study, to counteract the oxidative effects of DEHP, it is recommended to consume water-soluble antioxidants such as GA and CH or antioxidant-rich food products like black tea and dried fruits in small daily amounts.

Keywords: plant antioxidant, oxidative stress, bone marrow mesenchymal stem cells, Di(2-ethylhexyl) Phthalate, osteoblasts

Ps-82: Evaluation of the Effect of Curcumin-Au Nanoparticles on Pancreatic Islets Isolated from Rat

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Objective: Oxidative stress acts like rust on a delicate machine—it gradually damages the pancreatic islet cells responsible for insulin secretion. Curcumin, a natural compound with strong antioxidant properties, has shown promise in reducing this cellular damage. However, its low stability and poor bio-availability limit its direct application. To overcome this, the present study explores a novel approach using gold-curcumin nanoparticles (Cur-GNPs), synthesized through an eco-friendly (green) method, to enhance curcumin's effectiveness and stability. The main objective was to synthesize and characterize Cur-GNPs and investigate their impact on the viability and oxidative stress levels of isolated rat pancreatic islets.

Materials and Methods: Gold-curcumin nanoparticles were synthesized by reducing gold ions using curcumin in an aqueous medium—a green synthesis method akin to using nature's own toolkit. These nanoparticles were characterized through UV-Visible spectroscopy, Dynamic Light Scattering (DLS), Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES), and Transmission Electron Microscopy (TEM). Subsequently, pancreatic islets were isolated from rats using collagenase digestion followed by density gradient centrifugation. The purified islets were then cultured and treated with different concentrations of Cur-GNPs (20, 40, and 80 ppm) for one hour. Islet viability was assessed at 24, 48, and 72 hours using PI/FDA staining and fluorescence microscopy. Additionally, the intracellular reactive oxygen species (ROS) levels were measured using the DCFH-DA assay.

Results: The synthesized nanoparticles were spherical with a size range of 16–20 nm and showed high stability. DLS confirmed slightly larger hydrodynamic diameters due to surface charge and water molecule interactions. TEM analysis provided detailed morphological confirmation, and ICP-OES quantified the gold content precisely. Viability assays revealed no significant cytotoxic effects of Cur-GNPs on pancreatic islets at any tested concentration. More importantly, the DCFH-DA assay showed a noticeable reduction in intracellular ROS levels in treated groups, with the 40 ppm concentration demonstrating the most effective antioxidant response. These findings suggest that Cur-GNPs are not only biocompatible but also effectively reduce oxidative stress, highlighting their potential as protective agents in pancreatic islet preservation and possibly in diabetes-related applications.

Conclusion: In this study, we found that the nanoparticles we synthesized can improve the viability and functionality of isolated rat pancreatic islets, which could lead to better outcomes in vivo.

Keywords: Nanoparticle, Diabetes, Islet transplantation, Curcumin

Ps-83: Polycaprolactone/ Gelatin/ Layered Double Hydroxide Nanofibrous Scaffold Drug Delivery System for the Treatment of Melanoma Skin Cancer

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Objective: Nowadays, the use of drug delivery systems based on nanoparticles has expanded in the treatment of cancer, which can improve the efficiency of treatment to a great extent. The

aim of this study was synthesizing a layered double hydroxide (LDH)/polycaprolactone (PCL)/gelatin (GEL) nanofibrous scaffold and then use it to facilitate the delivery of 4-methyl-7-hydroxycoumarin (hymecromone) drug to B16F10 cancer cells.

Materials and Methods: LDH/hymecromone nanohybrid was synthesized by co-precipitation method and combined with PCL/GEL polymer solution and electrospun. X-ray diffraction, scanning electron microscopy and energy dispersive X-ray spectroscopy were used to characterize, identify the phase, morphology and elemental composition of the scaffold, respectively. Cell viability and apoptosis were assessed using the MTT assay and Calcein AM/PI double staining kit, and were visualized and imaged using a confocal microscope.

Results: The characterization results showed that the LDH/hymecromone nanohybrid was properly synthesized and incorporated into the nanofibrous scaffold. It was also found that the incorporation of LDH nanoparticles into the PCL/Gel scaffold improved its mechanical strength and elongation at break. Confocal microscopy results showed that 72 hours of incubation of the cells with PCL/GEL/LDH/hymecromone scaffold showed a greater effect of the drug compared to 24 hours of incubation. In addition to confirming the confocal results, the MTT results also showed that the use of the PCL/GEL/LDH/hymecromone scaffold significantly reduced the viability of B16F10 cells.

Conclusion: It seems that PCL/Gel/LDH scaffolds with slow and sustained release and protection of the drug against degradation can be suitable candidates as drug delivery systems.

Keywords: PCL, GEL, LDH, nanofibrous scaffold, Drug Delivery Systems

Ps-84: Bioinformatics-Based Targeting of CTNNB1 to Promote ESC-Derived Cardiomyocyte Differentiation Using Five Candidate Compounds

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Objective: Heart failure has always been a significant human health issue. Heart transplantation from donors has not been an ideal solution due to complications related to immune rejection. To address this, cell therapy may represent the most promising approach for resolving tissue dysfunction. In this context, understanding molecular mechanisms is a crucial first step toward producing functional cardiomyocytes through stem cell differentiation.

Materials and Methods: In our study, we used the GSE18514 dataset from the GEO database to identify differentially expressed genes (DEGs) in cardiomyocytes compared to embryonic stem cells using GEO2R. To explore their interactions, we constructed a protein-protein interaction (PPI) network, and to identify key proteins, we applied the CentiScape plugin based on betweenness centrality. CTNNB1 was identified as a major barrier hub gene in cardiomyocyte differentiation from embryonic stem cells. Therefore, we retrieved its protein structure from the Protein Data Bank (PDB), and identified several potential chemical components from the LINCS_L1000 database to be used as candidate ligands. Docking simulations were performed using Molegro Virtual Docker (MVD) software.

Results: This study reports five novel candidate chemical compounds Chlorpropamide, Edaravone, Oprozomib, PF-04457845

and Zeranol that may promote cardiomyocyte differentiation by inhibiting CTNNB1 hub gene. These findings may represent an important step toward generating lab-grown hearts for transplantation therapy in the future.

Conclusion: CTNNB1 inhibition by these novel compounds shows promise for cardiomyocyte differentiation and future heart regeneration therapies.

Keywords: Transplantation therapy, Stem cell technology, differentiation, bioinformatics

Ps-85: Production of Anti-CD22 CAR-NK

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Objective: Chimeric antigen receptor (CAR)-based immunotherapy has emerged as a powerful tool against hematologic malignancies. In this study, we aimed to generate CD22-targeted CAR-NK92 cells for potential application in B-cell lymphoma therapy.

Materials and Methods: We initiated our work by modifying a pre-existing CAR construct targeting CD19 and CD22. The CD19 segment was removed via restriction enzyme digestion, and the backbone vector was ligated with CD22-specific primers. Following ligation, transformation was carried out using competent *E. coli*, and colony PCR was performed on the resulting colonies to screen for positive clones. Further validation was conducted via double digestion and gel electrophoresis to confirm the correct insertion.

Results: post-transfection and subsequently used to transduce the NK92 cell line. Transduction efficiency was assessed by evaluating GFP expression in NK92 cells via flowcytometry (85%), indicating successful integration of the CD22-CAR construct.

Conclusion: Our workflow successfully generated CD22-CAR-expressing NK92 cells using lentiviral transduction, with GFP serving as a reporter of transgene expression. This model offers a promising approach for further investigation of CAR-NK therapy targeting CD22-positive malignancies.

Keywords: CAR-NK, CAR-T, CD22, Lymphoma,

Ps-86: Self-pumping Biomaterials for Wound Healing and Skin Regeneration: A Systematic Review

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Objective: Wound healing is one of the most important medical issues occurring due to the injuries or diseases. Various wound dressings with advanced physio-mechanical properties have been fabricated for this purpose. Among these biomaterials, self-pumping structures with their capability of exudates drain-

ing from wounds and promote skin repair by stimulating cellular and molecular mechanisms involved in the regeneration process so these dressings have attracted attentions in recent decades.

Materials and Methods: We accomplished this systematic review study using databases including Google scholar, Scopus, and PubMed. Studies published between 2022 and 2025 were included, focusing on the role of self-pumping dressing on skin tissue engineering and wound healing regeneration.

Results: Self-pumping wound dressings are often made by electrospinning, and in some studies, freeze-drying or a combination of both methods have been used to produce these wound dressings. These wound dressings can be two-layered or three-layered, consisting of a hydrophobic layer and a hydrophilic layer, and this layer can be made of hydrogel or nanofibers. Based on the amount of wound exudate, different drugs such as curcumin and antibacterial agents can be loaded inside the layers, and micro- or nanoparticles such as PLGA and microspheres can also be used to enhance the effectiveness of the drug and increase its effectiveness. The use of drugs can stimulate cellular and molecular processes in the healing process. In addition, in order to increase the effectiveness of these types of wound dressings, they can help to release as much exudate as possible by creating pores or aligned channels in the layers. These dressings can change the polarity of macrophages in the inflammatory phase by removing exudates and ROS, as well as increasing angiogenesis, proliferation of fibroblast cells, growth of hair follicles, and increasing collagen production for skin repair.

Conclusion: This systematic review has highlighted the promising prospects of self-pumping materials in wound healing application. More studies are needed to use these engineered material in large animal models and subsequently human clinical trials.

Keywords: Self-pumping Biomaterials, Wound Healing, Molecular and Cellular Mechanisms, Exudates draining

Ps-87: Mouse Animal Model Of Bacterial Keratitis Via Staphylococcus Aureus

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Objective: Corneal keratitis is a significant ocular condition that can lead to vision impairment if left untreated. While human studies offer valuable clinical insights, murine models play a crucial role in elucidating disease mechanisms and assessing therapeutic interventions. Murine models have been demonstrated to offer significant insights into the pathophysiology of corneal keratitis and the evaluation of therapeutic interventions. The objective of this study is to establish a standardized protocol for inducing corneal keratitis in mice to facilitate reproducible experimental outcomes.

Materials and Methods: Twelve-week-old male BALB/c mice were employed as the experimental model. Corneal infections were induced by creating superficial incisions arranged in different patterns and numbers with a 30-gauge needle, followed by topical application of a 20µl suspension containing 2×10^9 CFU of *Staphylococcus aureus*. Following 72 hours, the mice were euthanized and the eyes were evaluated both macroscopically and microscopically using a slit lamp biomicroscope.

Corneal turbidity was detected with fluorescein. Then, the mice were killed by cervical dislocation, and eyes were enucleated and homogenized in 1.0 mL sterile phosphate buffered saline (PBS) with sterile glass stirring rod. The homogenate was plated into TSA and incubated at 37°C for 24 hours. Finally, the colonies were counted and colony-forming units (CFU)/cornea were reported.

Results: At post infection (PI) day 3, no pathologic changes were observed in BALB/c mice with three parallel scratch and corneas were clear. On the other hand, some corneal opacity was observed in mice with six scratches in crosswise pattern when the eyes were analyzed by fluorescein staining under blue light using OMS-90 operation microscope. In the three parallel scratch model, bacterial colonies were absent. However, the number of CFU recovered from infected eyes of six-scratch crosswise pattern model was found 2.2×10^3 CFU.

Conclusion: This model functions as a foundational framework for the study of corneal infections and the testing of novel therapeutic approaches in ophthalmic research.

Keywords: Bacterial Keratitis, Animal Model, Staphylococcus aureus

Ps-88: The Effect of A Novel Nano Drug Delivery System Encapsulating A Gut Microbiota-Derived Metabolite on A 3D Biomimetic Gastric Cancer Model

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Objective: Gastric cancer is a major cause of cancer-related mortality worldwide, often associated with limited treatment response, therapy resistance, and recurrence. Targeted therapeutic approaches utilizing advanced nanotechnology and tissue-relevant in vitro systems have emerged as promising strategies for improving drug delivery and therapeutic specificity. However, challenges remain in bridging in vitro findings with physiologically relevant tumor responses.

Materials and Methods: In this study, a nanotechnology-based formulation was developed to assess its impact on a laboratory-generated three-dimensional cancer model that more closely mimics the in vivo tumor microenvironment. A variety of molecular and cellular techniques were used to evaluate cell phenotype, gene and protein expression, and cell behavior in response to treatment. Standard biophysical characterization methods were employed for validating the nanoformulation properties. Characterization assays included DLS, zeta potential, and encapsulation efficiency. Cytotoxicity, gene and protein expression (via qRT-PCR, Western blot, and Immunostaining), and functional assays (Live/Dead, MTS, and Migration) were performed to assess treatment efficacy.

Results: The results demonstrated significant phenotypic modulation in the treated cancer model. Rather than inducing overt cytotoxic effects, the treatment led to changes in cell morphology and molecular marker expression suggestive of reduced malignancy and a more differentiated cellular phenotype. These findings were supported by changes in epithelial and mesenchymal marker expression, consistent with therapeutic reprogramming effects.

Conclusion: Our findings highlight the potential of using advanced nano drug delivery in combination with 3D cancer models to explore novel therapeutic strategies aimed not only at eliminating cancer cells, but also at modulating their behavior toward a less aggressive phenotype. This approach may contribute to the development of safer, differentiation-oriented therapies for solid tumors.

Keywords: 3D Cancer Model, Differentiation Therapy, Nano Drug Delivery, Gastric Cancer, Microbiota

Ps-89: Targeting the Achilles' Heel of Cancer: Advances in Understanding and Eradicating Therapy-Resistant Cancer Stem Cells

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Objective: Cancer stem cells (CSCs) are pivotal in tumor recurrence and therapeutic resistance, primarily due to their adaptive capacity within the tumor microenvironment (TME). This microenvironment, comprising immune cells, stromal components, and vasculature, sustains CSC stemness. While CSC heterogeneity complicates treatment, it unveils novel targeting opportunities. Cutting-edge single-cell sequencing and multi-omics approaches are deepening our understanding of CSC behavior under influences like hypoxia.

Materials and Methods: This systematic review (2019–2024) searched PubMed, Scopus, Web of Science, and Google Scholar using AI-assisted Boolean operators (AND/OR). Search strategies combined CSC-related terms ("cancer stem cells" OR "tumor-initiating cells") with: • Technique keywords ("single-cell sequencing", "multi-omics") • Microenvironment factors ("hypoxia", "tumor microenvironment") • Therapeutic approaches ("immunotherapy", "CAR-T cells", "monoclonal antibodies", "CSC vaccines") • Detection/delivery methods ("liquid biopsy", "exosome biomarkers", "surface markers", "nanoparticle drug delivery"). From 1, 200 identified records, 250 articles underwent title/abstract screening using inclusion criteria (English, original research). 38 eligible studies were selected for full-text analysis.

Results: Innovative single-cell and multi-omics approaches uncovered extensive genetic and functional heterogeneity among CSCs. Preclinical studies demonstrate that: • Immunotherapies targeting CSC-specific markers (CD44, CD133) including CAR-T cells and monoclonal antibodies • Inhibition of key signaling pathways (Hippo/YAP, Jak/STAT3) significantly impede CSC-mediated tumor progression. Novel liquid biopsy biomarkers enable early CSC detection and monitoring, while nanoparticle-based strategies show increased therapeutic speci-

ficity and reduced systemic toxicity in experimental models.

Conclusion: Despite substantial progress in CSC profiling and targeted therapies, challenges including CSC plasticity, heterogeneity, and lack of exclusive markers persist. Ongoing advances in multi-omics, bioinformatics, and combination therapies hold promise for overcoming these barriers and improving cancer treatment outcomes.

Keywords: Cancer stem cells (CSCs), Tumor microenvironment, Single-cell multi-omics, Targeted immunotherapy

Ps-90: Cell-Based Approaches for Ureteral Tissue Engineering: Stem Cell Strategies and Applications

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Objective: Ureteral abnormalities due to malformation, trauma, or treatment unknown damage represent a significant clinical problem for Urologists. traditional surgical repair often involves limited access to autografts and includes complications from stenosis and fibrosis. The use of stem cells with biocompatible scaffold constructs for tissue engineering presents a potential alternative to conventional surgical repairs. This review encompasses the development of stem cell-based strategies, scaffold designs, and outcomes for uses of previous studies.

Materials and Methods: Stem Cell Sources: Stem cell lines used in studies include Urine-derived stem cells (USCs), adipose-derived stem cells (ADSCs), and bone marrow-derived mononuclear cells (BM-MNCs) which were used to differentiate into urothelial and smooth muscle cells and improve angiogenesis. Scaffold Design: The use of natural scaffolds such as decellularized porcine ureters and vascular extracellular matrix (VECM) treated with detergents. Hybrid scaffolds that included both synthetic and nature materials of PLA/collagen and seamless tubular collagen were also investigated. Crosslinking agents such genipin (GP), and carbodiimide (CDI) were used to improve biocompatibility and structural stability. In Vitro and In Vivo Models: Differentiated cells were seeded onto scaffolds using dynamic culture systems. Animal models, including rabbits and rats, were used to assess graft vascularization, patency, and integration.

Results: USCs and ADSCs differentiated successfully, expressing urothelial and smooth muscle markers (CK-7, α -SMA, SM-MHC). Scaffolds supported cell infiltration and tissue formation, with crosslinked scaffolds showing superior integration. In vivo studies confirmed vascularization and organized tissue structure. BM-MNCs and cardiomyocyte sheets further enhanced angiogenesis and patency.

Conclusion: Stem cell-based tissue engineering, particularly using USCs and ADSCs, shows strong potential for ureteral reconstruction. Further studies are needed to optimize scaffold design and facilitate clinical translation.

Keywords: Ureteral tissue engineering, Stem cells, Regenerative medicine, Scaffolds

Ps-91: Growth Factor-Loaded Chitosan Microneedle Patches Stimulated Angiogenesis in in vitro and in vivo

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Objective: The development of sophisticated delivery systems has been at the center of attention in recent years. Microneedle patches are platforms for the delivery of various cargoes into the target tissues with highly efficient delivery capacities. Here, the possible angiogenesis properties of VEGF-loaded chitosan-based microneedle patches were monitored in an in vitro laboratory system and in vivo.

Materials and Methods: Chitosan microneedle patches were fabricated using silicon micromolds with typical needle array features, and different physicochemical properties evaluated by SEM and different assays. For angiogenesis evaluation, VEGF were loaded in the needle backbone during the casting, and the survival rate of HUVECs was monitored 48 hours after being exposed to VEGF-loaded microneedle patches. The possible toxicity and vascularization capacity was assessed in mice after being placed into the subcutaneous space using surgical approaches.

Results: SEM assays revealed the typical features of needles with certain geometries (Heights: 800, Base diameter: 600, and tip diameter: 20 μ m) which are suitable for local growth factor delivery. Along with these features, appropriate mechanical properties were documented for the designed microneedle patches. Histological examination revealed the lack of local and systemic toxic effects coincided with the stimulation of vascularization to the target sites.

Conclusion: Taken together, these data indicate that microneedle patches are valid platforms for the stimulation of angiogenesis with specific loaded growth factors.

Keywords: Microneedle patch, HUVECs, Angiogenesis, Releasing platform, Toxic effects

Ps-92: From Data to Delivery: A Systematic Review of Artificial Intelligence-Driven Innovations in Medical Nanotechnology

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Objective: Background: Medical nanotechnology holds promise for revolutionizing diagnostics, targeted therapy, and regenerative medicine at the nanoscale but faces challenges including complex nano-bio interactions, optimizing targeted delivery, lengthy development and validation processes, high

costs, and uncertainty in predicting in vivo efficacy and safety. Meanwhile, artificial intelligence (AI) has transformed medical research and engineering by enabling data-driven design, predictive modeling, and process automation. Integrating AI into medical nanotechnology can accelerate discovery, enhance design optimization, and reveal insights from large, complex datasets. This systematic review aims to evaluate the current role and contributions of AI in developing, optimizing, and applying medical nanotechnology.

Materials and Methods: A systematic search of PubMed was conducted for articles indexed with “artificial intelligence,” “machine learning,” “deep learning,” and at least one of “medical nanotechnology” or “nanomedicine” between January 1, 2023, and May 31, 2025.

Results: The initial search retrieved 326 articles. A single reviewer screened titles, abstracts, and full texts, applying pre-defined inclusion and exclusion criteria, yielding a final set of relevant studies. Analysis revealed that AI has been extensively applied to optimize nanoparticle design and formulation, predict nanotoxicity and biocompatibility, accelerate nanodrug discovery and delivery system development, enhance nano-imaging analysis, and advance nanosensor and nanodiagnostic capabilities.

Conclusion: The integration of novel AI frameworks in medical nanotechnology is increasingly necessary to reduce uncertainty, lower development costs and timelines, improve predictive accuracy for performance and safety, enable personalized nanomedical interventions, and facilitate successful clinical translation of nanotechnology products.

Keywords: Medical Nanotechnology, Artificial Intelligence, Machine Learning, Deep Learning, Nanomedicine

Ps-93: Artificial Intelligence–Driven Advances in Tissue Engineering: A Systematic Review of Current Applications and Future Prospects

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Objective: Tissue engineering aims to regenerate or repair damaged tissues and organs but continues to face major obstacles, including the complexity of biological systems, extended development timelines, high costs, and variability in outcomes. Artificial Intelligence (AI), with its capacity to analyze vast datasets and automate complex tasks, is emerging as a transformative force across biomedical fields. Since the early 2000s, AI has increasingly been integrated into tissue engineering to optimize scaffold design, predict cell behavior, and streamline fabrication techniques. This systematic review aims to explore the current state, applications, and future potential of AI in advancing tissue engineering.

Materials and Methods: A systematic search was conducted in the PubMed database for English-language articles published from January 1, 2023, to January 1, 2025. Keywords included "artificial intelligence," "machine learning," "deep learning," and at least one of "tissue engineering," "scaffold fabrication," or "cell engineering." A single reviewer screened the titles and abstracts to identify studies aligning with predefined eligibility criteria. Relevant data were extracted from eligible full-text articles and categorized based on AI techniques and applications.

Results: The initial search retrieved 299 articles. Preliminary analysis reveals a rising trend in the use of AI across diverse domains of tissue engineering. Applications range from scaffold microarchitecture optimization and cell behavior prediction to improving bioprinting accuracy and enhancing image-based tissue modeling. The studies highlight both the promise and variability in outcomes of current AI-driven approaches.

Conclusion: AI is poised to play a pivotal role in the evolution of tissue engineering. Its implementation can accelerate discovery, reduce experimental costs and time, and enhance predictive accuracy. By enabling more personalized and precise solutions, AI has the potential to significantly improve the clinical translation of engineered tissue products.

Keywords: Tissue Engineering, Artificial Intelligence, Machine Learning, Deep Learning, Scaffold Fabrication

Ps-94: Localized Delivery of GDNF via PLGA Microparticles Enhances 3D Culture Expansion of Mouse Spermatogonial Stem Cells

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Objective: Three-dimensional (3D) culture systems provide a more biomimetic environment for stem cell growth compared to two-dimensional (2D) models. However, limited diffusion of growth factors within dense 3D aggregates often hampers efficient cellular signaling. To address this, localized delivery of growth factors via polymeric microparticles has emerged as a promising strategy. This study aimed to enhance the proliferation of mouse spermatogonial stem cells (SSCs) through the localized delivery of glial cell line-derived neurotrophic factor (GDNF) using PLGA microparticles incorporated into an alginate hydrogel scaffold.

Materials and Methods: GDNF-loaded PLGA microparticles were fabricated using a modified double emulsion technique optimized to minimize initial burst release. These microparticles were incorporated into alginate hydrogels and applied to 3D SSC cultures. SSC proliferation and gene expression of key stemness markers (Ki67, GFR α 1, and Oct4) were evaluated through MTS assay, qRT-PCR, and immunofluorescence analysis.

Results: Gene and protein expression analyses demonstrated significant upregulation of Ki67, GFR α 1, and Oct4 in SSCs treated with GDNF-loaded microparticles compared to SSCs cultured with soluble GDNF. Moreover, sustained release of GDNF from microparticles effectively supported SSC proliferation over time.

Conclusion: Localized and sustained delivery of GDNF via PLGA microparticles embedded in alginate scaffolds provides a superior strategy to enhance SSC expansion under 3D culture

conditions. This platform offers potential applications for fertility preservation and regenerative medicine.

Keywords: Spermatogonial stem cells, 3D cell culture, Growth factor delivery, PLGA microparticles, Alginate hydrogel

Ps-95: Spermatogonial Stem Cells in the Treatment of Azospermia

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Objective: Azospermia, the most severe form of male infertility, is characterized by the complete absence of sperm in semen and affects approximately 1% of men. It results from disrupted spermatogenesis caused by hypothalamic-pituitary axis dysfunction, primary testicular failure, or obstruction of the reproductive tract.

Materials and Methods: The authors performed a research investigation in PubMed and Google Scholar using the three search terms azospermia, spermatogonial stem cells and spermatogenesis. The research examined scholarly articles which were published throughout 2013 to 2023.

Results: The two types of Azospermia present as obstructive and non-obstructive but non-obstructive cases develop due to testicular dysfunction. Healthcare providers use FSH, LH and testosterone hormonal tests together with semen analysis, scrotal ultrasound imaging and testicular biopsy for accurate diagnosis. The spermatogenesis lifecycle extends indefinitely due to SSCs located beneath the base of seminiferous tubules. Research conducted on animals has shown that transferring SSC cells into testes devoid of germ cells results in natural sperm production recovery. SSCs are extracted by enzymatic treatment such as trypsin and collagenase before sorting thus allowing them through magnetic or fluorescence-activated cell sorting. Short-term culture of SSCs becomes possible by using the rete testis or efferent ducts for their delivery. Testicular delivery through the rete testis results in equal distribution of cells which leads to successful tubule penetration. The techniques for successful SSC colonization and spermatogenesis initiation were proven effective through studies conducted on three different species including mice and primates and dogs.

Conclusion: Through SSC transplantation doctors can provide a specific method to restore fertility capabilities in patients who have no sperm. Research indicates that this method will likely establish a connection between laboratory modeling and medical applications of fertility treatment for male patients.

Keywords: Azospermia, Spermatogonial Stem Cells (SSCs), Spermatogenesis, Male Infertility, Stem Cell Transplantation

Ps-96: Electrical Shock-Triggered Schwann Cell Phenotypic Conversion as a Potential Strategy for Nerve Regeneration

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Objective: Electrical injuries often cause severe nerve damage, leading to chronic pain and sensory loss. Traditional views suggest limited nerve regeneration, but recent studies high-

light cellular reprogramming as a potential solution. This case study examines a 45-year-old male with electrical burns, where Schwann cells—typically responsible for nerve support—transformed into nociceptive-like neurons. This phenotypic shift, driven by electrical stimulation and paracrine signals (e.g., FGF2, ATP), challenges conventional nerve repair paradigms and opens new therapeutic avenues.

Materials and Methods: The study combined clinical, electrophysiological, and molecular analyses. Neurological exams assessed sensory deficits, while nerve conduction studies detected action potentials in reprogrammed Schwann cells. Tissue biopsies underwent immunohistochemistry to confirm loss of Schwann markers (S100 β , MBP) and gain of neuronal markers (β -III-tubulin, Nav1.8). Chromatin remodeling and paracrine signaling were analyzed via ChIP assays and ELISA. Imaging techniques (confocal/electron microscopy) visualized structural changes and synaptic connections.

Results: Electrophysiology revealed functional activity in transformed Schwann cells, which expressed neuronal markers and formed synapses with epithelial cells. Histology confirmed complete neuronal loss but identified Schwann cell-derived neuron-like cells. Molecular analysis showed chromatin remodeling and elevated FGF2/ATP levels, suggesting their role in reprogramming.

Conclusion: Electrical injury can induce Schwann cell transdifferentiation into functional neurons, offering a groundbreaking strategy for nerve regeneration. Targeted electrical stimulation or nanoparticle-based therapies could harness this mechanism clinically. Further research is needed to optimize these approaches for human applications.

Keywords: Nerve regeneration, Schwann cells, neuroplasticity, electrical injury, cellular reprogramming

Ps-97: The Potential of CRISPR/Cas9 Gene Editing Technology to Treat Type 2 Diabetes

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Objective: Type 2 diabetes, also known as adult-onset diabetes, is one of the most prevalent metabolic disorders among adults. The therapeutic strategies, as discovered until today, are potentially ineffective or accompanied by side effects. Accordingly, it is certainly crucial to aim for more advanced and practical treatments. Gene therapy is a kind of treatment that fixes gene defects by replacing or disrupting them and clustered regularly interspaced short palindromic repeats CRISPR-associated protein 9 (CRISPR/Cas9) editing technology is a promising technique in this field of study. For this review, we provide an investigation into the usage of CRISPR/Cas9 to cure type 2 diabetes.

Materials and Methods: We conducted an extensive search across electronic databases, including PubMed, Medline, Google Scholar, and ResearchGate, and explored the available English-language literature. The mesh terms were “Type 2 diabetes”, “CRISPR/Cas9”, and “Gene therapy”.

Results: CRISPR/Cas9 has been tested for eliminating genes to optimize signalling of insulin. In a study, the researchers disrupted the dipeptidyl peptidase-4 (DPP-4) gene in mice. This enzyme contributes to the degradation of glucagon-like peptide-1 (GLP-1), which helps the secretion of insulin. The disruption of the so-called gene was operated by CRISPR/Cas9,

and it resulted in improved insulin response.

Conclusion: With all the limitations the CRISPR-Cas9 gene editing system holds, it still can be a favourable therapy for type 2 diabetes. Generally, gene therapy carries a high probability of replacing the genes that are causing insulin signalling dysfunction with healthy genes.

Keywords: Type 2 diabetes, CRISPR/Cas9, Gene therapy

Ps-98: The Effects of Lithium on the Activity of Wnt and BMP Signaling Pathways During Osteogenic Differentiation of Adipose – Derived Mesenchymal Stem Cells

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Objective: Osteoporosis is one of the most common bone disorders that many people, especially the elderly, suffer from all over the world. Although bone is a tissue that has the ability to repair itself, during osteoporosis, a large part of the bone mass is depleted and causes fractures. There are several treatment options for this injury, including the use of drugs, surgery of the damaged parts, bone grafts, and the use newest approach of tissue engineering and stem cells therapy. Most of the above options have side effects and limitations like enhancement of osteosarcoma, lack of donors, infection and immune reactions, high costs, and failure to repair large lesions. However, the use of stem cells as a renewable source that does not transmit diseases and has anti-inflammatory and modulatory properties is highly recommended. Among the various sources of stem cells, adipose tissue-derived mesenchymal stem cells (AD-MSCs) are a better choice due to their easier access and isolation. During the control of stem cell activities, cellular signaling pathways play important role, among which the Wnt pathway plays a decisive role in bone formation. In the first stage of this study, we determined the role of Wnt signaling pathway in the osteogenic differentiation of AD-MSCs by using lithium chloride as an activator of the Wnt pathway. There is a lot of evidence that Wnt signaling has interactions with other cellular pathways such as BMP, which can affect them and lead to a change in the osteogenic differentiation pathway. Therefore, we investigated the possible interaction of the Wnt pathway with the BMP pathway in the osteogenic differentiation process of mesenchymal stem cells.

Materials and Methods: To determine a non-toxic concentration of lithium suitable for the cells, an MTT assay was performed. A real-time PCR assay was performed due to the activation of the Wnt signaling pathway by lithium. To investigate the effect of LiCl on the osteogenic potential of Ad-MSCs, cells were constantly exposed to 10 mM LiCl, while they were kept in the osteogenic induction medium. The expression of osteogenic-related genes ALP, runt related transcription factor 2 (RUNX2) and OPN (Osteopontin) was measured by real-time PCR. Osteogenesis was then qualified by measurement of the amount of matrix mineralization by Alizarin Red staining and calcium content assay.

Results: Results indicated that the adipose-derived mesenchymal stem cells in 10 mM lithium concentration maintained healthy growth however the effect of lithium on the cells, compared to the control group, resulted in a decreased activation of the Wnt signaling pathway as well as reduced osteogenic differentiation.

Conclusion: Lithium chloride causes differentiation inhibition.

Keywords: Lithium chloride, Osteogenesis, Mesenchymal stem cells, Wnt pathway

Ps-99: Comparing the Impact of 3D and 2D Culture System on Immunomodulation Potency of Bone Marrow Derived-Clonal MSCs

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Objective: Mesenchymal stem cells (MSCs) hold great therapeutic promise due to their regenerative and immunomodulatory abilities. However, scaling up production while maintaining quality is challenging with traditional 2D cultures. Bioreactors offer precise control over growth conditions, enabling reliable, large-scale manufacturing of high-quality MSCs. Current efforts focus on standardizing protocols and optimizing cost-effective methods to transition MSC therapies from the lab to widespread clinical use.

Materials and Methods: MSCs were expanded in a DASbox bioreactor under normoxia (100% DO) and hypoxia (20% DO), then co-cultured with activated PBMCs (1:2 and 1:10 ratios) for LPA to assess immunosuppression. For in vivo testing, they were intravenously injected into inflamed BALB/c mice (control, sham, treatment groups). Blood and tissues (liver, kidney, lung) were analyzed.

Results: Hypoxic MSC expansion in the DASbox bioreactor yielded 9×10^7 cells in 12 days with enhanced immunomodulation. Improved microcarrier adhesion under hypoxia (with optimized agitation) significantly boosted proliferation while reducing medium consumption by $2.5 \times$ versus 2D cultures, lowering industrial-scale costs. CFSE-based flow cytometry showed hypoxic MSCs suppressed PBMC proliferation as effectively as negative controls. In septic mice, hypoxic MSC treatment normalized acute inflammation (reduced neutrophils), lowered elevated urea/creatinine, and restored TNF- α /IL-2/IFN- γ to near-control levels.

Conclusion: Large-scale bioreactor systems are crucial for scalable, reproducible, and regulatory-compliant production of MSCs. Advanced PAT-enabled platforms enable real-time monitoring of critical quality attributes, ensuring consistency and clinical-grade standards.

Keywords: Mesenchymal stromal cell, Bioreactors, Hypoxia, Dynamic culture

Ps-100: Biocompatibility Assessment of Electrospun PVA–Organum Vulgare Fibers Using HDF Cells

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Objective: Tissue engineering aims to repair and restore the function of damaged tissues using cells, scaffolds, and bioactive molecules. Biopolymeric materials are of significant inter-

est in scaffold fabrication due to their inherent biocompatibility and therapeutic properties. Among various fiber production techniques, electrospinning uniquely enables the fabrication of scaffolds with structures closely resembling the extracellular matrix (ECM), producing fibers ranging from the nano- to microscale. In this study, biocompatible fibers composed of polyvinyl alcohol (PVA) and *Origanum vulgare* extract were fabricated via electrospinning and evaluated for biomedical applications. Water-soluble PVA was used as the scaffold base, while *Origanum vulgare* extract—rich in anti-inflammatory and antioxidant bioactive compounds—was incorporated to enhance both structural support and tissue healing.

Materials and Methods: A 10 wt% PVA solution was prepared by heating to 80°C and then cooled to room temperature. *Origanum vulgare* extract was obtained through hydroalcoholic extraction and rotary evaporation, and added to the polymer solution at a defined weight ratio. Electrospinning was performed under standardized conditions: 20 kV applied voltage, ambient temperature of 23°C, and relative humidity of 47%. Fiber morphology was analyzed using SEM, while FTIR was used to evaluate interactions between functional groups. Cytotoxicity was assessed via MTT assay using human HDF cells seeded at a density of 5000 cells per well in 96-well plates, with exposure durations of 24 and 48 hours.

Results: SEM imaging revealed uniform, bead-free fibers with average diameters of 27, 30, and 36 µm. FTIR spectra displayed sharp peaks in the wavenumber ranges of approximately 2900 and 3286 cm⁻¹, indicating interactions between hydroxyl groups in PVA and phenolic compounds in *Origanum vulgare*. MTT assay results showed no cytotoxic effects on HDF cells at either time point.

Conclusion: Electrospun PVA scaffolds incorporating *Origanum vulgare* extract exhibited high biocompatibility and porosity. In addition to offering protection against oxidative stress and inflammation, the scaffolds also promoted the proliferation of skin fibroblasts. These findings suggest potential for future applications in wound healing and tissue regeneration studies.

Keywords: Electrospinning, *Origanum vulgare*, HDF cell line, Polyvinyl alcohol

Ps-101: PPIG and EPRS Hub Genes Identified as Targets to Parkinson's Disease Via Bioinformatics Approaches

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Objective: Parkinson's disease (PD) is a progressive neurological disorder that primarily negatively affects movement control, caused by the reduction of dopaminergic neurons in the brain. Despite extensive research, the molecular mechanisms underlying this disease remain unanswered.

Materials and Methods: This study aims to report a comprehensive analysis of differentially expressed genes (DEGs) in Parkinson's patients compared to healthy individuals. We utilized the Gene Expression Omnibus (GEO) database with access number GSE150696, where we identified 1455 differentially expressed genes, including 674 upregulated genes and 781 downregulated genes. Using protein-protein interaction (PPI) analysis with the STRING database and the Cytoscape program, we identified the top twenty hub genes involved in

Parkinson's pathology.

Results: In further investigations, we identified two novel hub genes, PPIG and EPRS, which had not been previously studied in Parkinson's research and could potentially be recognized as new therapeutic targets.

Conclusion: These findings enhance our understanding of the molecular aspects of Parkinson's disease and provide a new era for implementing targeted therapies. By advancing therapeutic strategies, genetic analysis, and the exploration of new biomarkers, future studies could contribute to more advanced treatment strategies.

Keywords: Parkinson's Disease, Gene Expression, Microarrays, Bioinformatics, Hub genes

Ps-102: Sustained And Localized Delivery of Retinal Pigment Epithelial Cells-Derived Factors by Peg-Based Bioadhesive for Regenerative Repair of Retinal Detachment

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Objective: Retinal detachment is a severe eye condition that can result in irreversible vision loss due to the degeneration of photoreceptors. Standard treatments often fail in extensive cases or with macular holes. There is an urgent need for novel approaches that provide both tissue adhesion and cellular protection to improve surgical outcomes. This study evaluates a polyethylene glycol (PEG)-based adhesive hydrogel loaded with growth factors secreted by retinal pigment epithelium (RPE) cells as a regenerative tissue adhesive.

Materials and Methods: Hydrogel formulations were prepared using various molar ratios of amine (NH₂) and succinimidyl ester (NHS) derivatives of 4arm-PEG (1:1, 1:1.5, 1:2, and 1:3). Adhesion strength was measured via lap shear test, while mechanical compatibility was assessed through compression testing to determine the elastic modulus. The hydrogel biodegradability in BSS was monitored over 26 days and protein release profile was determined by BCA kit. Cytocompatibility was evaluated by MTS assay in a normal retinal ganglion cell line. To model disease conditions, the retinal ganglion cell line was subjected to oxidative stress induced by tert-butyl hydroperoxide (TBHP). The bioactivity of incorporated growth factors was assessed by their ability to mitigate cell death under the inflammatory conditions.

Results: The PEG hydrogel with a 1:2 molar ratio of NH₂/NHS exhibited superior adhesive strength (145±3.034 kPa), proper biodegradation rate (over 7 days), and a tissue mimetic elastic modulus of 10.1±1.109 kPa. Cytotoxicity assays confirmed biocompatibility, while growth factor-loaded hydrogels significantly reduced cell death in oxidative stress modeled cells, demonstrating neuroprotective effects.

Conclusion: The PEG-based hydrogel loaded with RPE-derived growth factors showed promise as a regenerative retinal tissue adhesive, providing mechanical stability, biodegradability

ity, and neuroprotection. These findings suggested its potential application in complex retinal detachment cases, including those involving macular holes.

Keywords: tissue adhesive, retinal repair, Retinal detachment, polyethylene glycol, growth factors

Ps-103: Neuroprotective Effects of Mesenchymal Stem Cell-Derived Exosomes: A Systematic Review of Experimental Studies

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Objective: Neurological disorders, including stroke, Alzheimer's disease, and traumatic brain injury, are among the leading causes of death and disability worldwide. Exosomes derived from mesenchymal stem cells (MSC-Exos) have recently been identified as promising therapeutic agents due to their ability to cross biological barriers and deliver bioactive cargo that plays a role in neuroprotection, anti-inflammation, and regeneration. This systematic review consolidates experimental data regarding the neuroprotective effects of MSC-Exos in preclinical models.

Materials and Methods: A systematic literature search was conducted in PubMed, Scopus, and Web of Science databases for publications from January 2013 to May 2025. The search terms employed included "mesenchymal stem cell exosomes" in conjunction with "neuroprotection," "stroke," "traumatic brain injury," and "Alzheimer's disease." The inclusion criteria were original in vivo and in vitro studies that examined the neuroprotective effects of MSC-derived exosomes. Review articles and studies not related to neuronal research were excluded. Ultimately, a total of 11 original experimental studies were selected for final analysis after the screening process.

Results: 11 studies included demonstrated positive neuroprotective outcomes following MSC-Exos administration. These outcomes included the prevention of neuronal apoptosis, suppression of neuroinflammation, enhancement of synaptic plasticity, increased neurogenesis, and restoration of function in models of stroke, Alzheimer's disease, spinal cord injury, and traumatic brain injury. The MSC-Exos were sourced from bone marrow, umbilical cord, or adipose tissue and were administered via intravenous, intranasal, or direct intracerebral routes. Mechanistically, the exosomes exerted their effects through signaling pathways such as PI3K/Akt, PTEN/Akt, and SIRT1/AMPK, as well as through regulatory mechanisms involving microRNAs, including the miR-17-92 cluster.

Conclusion: MSC-derived exosomes exhibit consistent neuroprotective effects in models of neurological diseases. Their non-cellular biochemistry, low immunogenicity, and biological activity underscore their potential as novel therapeutic agents for future clinical applications in neurodegenerative and neuro-inflammatory disorders.

Keywords: Mesenchymal Stem Cell-derived Exosomes, Neuroprotection, Extracellular Vesicles, Systematic Review

Ps-104: Molecular Docking-Based Comparison of IGF-1 Agonists for Enhancing Stem Cell-Derived Neurogenesis

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Objective: IGF-1 signaling is essential for the survival, growth, and differentiation of neural stem and progenitor cells. While recombinant IGF-1 has neurogenic properties, its effectiveness is hindered by limited penetration of the blood-brain barrier and a short half-life. Small-molecule agonists that bind to the extracellular domain (ECD) of the IGF-1 receptor (IGF-1R) may overcome these challenges, enhancing stability and bioavailability for neuroregenerative therapies.

Materials and Methods: The structure of the IGF-1R ECD (PDB ID: 3LVP) was prepared using PyRx (AutoDock Vina) by removing water molecules and co-crystallized ligands. Polar hydrogens and Gasteiger charges were added, and the receptor was converted to PDBQT format. Three potential agonists—Resveratrol (CID 445154), Nordihydroguaiaretic acid (NDGA) (CID 4534), and Pirinixic acid (CID 5694)—were imported from SDF format, which automatically protonated, charged, and assigned rotatable bonds to them in PyRx. A cubic docking grid box (30 Å edge length) at (X=8.763 Å, Y=56.065 Å, Z=19.830 Å) encompassed the previously reported IGF-1 binding pocket. All ligands underwent 50 genetic algorithm runs using the default parameters for Vina. Published predictions of binding affinity (ΔG_{bind}) and hydrogen bond interactions were accessed from the "Analyze Results" tab in PyRx for comparison.

Results: Predicted ΔG_{bind} values and hydrogen bond counts for each agonist were: Resveratrol: $\Delta G = -7.2$ kcal/mol, H-bonds = 3 (interactions with Asp1123, Leu1097, Phe1168) NDGA: $\Delta G = -7.0$ kcal/mol, H-bonds = 1 (contact with Lys1270) Pirinixic acid: $\Delta G = -6.6$ kcal/mol, H-bonds = 2 (contacts with Tyr1213, Lys1250) Resveratrol exhibited the highest docking score and the greatest number of hydrogen bonds, demonstrating a strong ability to mimic IGF-1 binding. NDGA and Pirinixic acid displayed moderate affinities, suggesting potential interactions with the ECD.

Conclusion: Resveratrol has been identified as a prominent small-molecule agonist of the IGF-1R ECD and should be prioritized for in vitro receptor activation testing and subsequent neurogenic assays. Additionally, NDGA and pirinixic acid demonstrated positive interactions and may serve as alternative modulators. These in silico findings provide a strong rationale for developing small-molecule strategies to enhance IGF-1-mediated neurogenesis.

Keywords: IGF-1R, Resveratrol, Nordihydroguaiaretic acid, Pirinixic Acid, Molecular Docking

Ps-105: Optimization of Preservation of Keratinocyte Sheets

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Objective: Chronic wounds, which fail to heal and stay in the inflammatory phase, mainly include pressure, diabetic, venous, and arterial ulcers. Their global prevalence is about 1.67 per 1,000 people, with elderly individuals (ages 70–80) being most affected. Treating chronic wounds is a major healthcare challenge. One promising method is using biological skin substitutes, but this faces obstacles especially in long term preservation. Cryoprotectants, used to store these products, can harm cells by causing cytotoxicity and osmotic stress, particularly at high concentrations or temperatures. Each cryoprotectant behaves differently depending on the cell type and experimental conditions, making preservation complex. Additionally, cryopreservation needs expensive equipment to maintain ultra low temperatures, which limits its practical use. This research aims to create a new storage method for living cells and tissues that reduces damage and simplifies transportation.

Materials and Methods: In line with the objectives of this research, the study will be conducted in a single in vitro phase. During this phase, the keratinocyte sheet will be prepared according to a standardized protocol. Subsequently, to confirm the functionality of the product, the following quality control tests will be performed: • Hematoxylin and Eosin (H&E) staining to evaluate the structural integrity of the sheet. • Immunohistochemistry to examine the expression of K10 and K14 markers, which are essential for wound healing. This study includes three Deep Freezing groups: 1. Frozen keratinocyte sheet with DMSO as the cryopreservation medium 2. Frozen keratinocyte sheet with glycerol as the cryopreservation medium 3. Frozen keratinocyte sheet with removal cryopreservation medium After one month of storage, QC tests will be conducted on all groups. **Results:** 1. The keratinocyte sheet produced was approved based on quality control tests. 2. The H&E staining confirmed the overall morphology of the sheet after freezing. 3. The immunohistochemistry test confirmed the presence of K14⁺ and K10⁺ cells.

Conclusion: In this study, we found that our optimized freezing environment, which includes the removal of freezing medium, can perform better than the conventional freezing method.

Keywords: Deep Freezing, Keratinocyte Sheet, Optimization, Storage Methods

Ps-106: Design And Development of A Gelatin-Based Metamaterial Hydrogel Containing Zinc Oxide Nanoparticles and Paclitaxel for Glioblastoma Cell Elimination

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Objective: Glioblastoma is a highly invasive brain tumor with poor prognosis and limited treatment options, mainly due to drug resistance, recurrence, and the blood-brain barrier. In this study, we developed a novel gelatin-based metamaterial hydrogel incorporating chitosan-coated zinc oxide (ZnO) nanoparti-

cles, aiming to create a biodegradable and biocompatible platform localized therapy.

Materials and Methods: The hydrogel was fabricated using gelatin and synthesized ZnO nanoparticles. Characterization analyses included FTIR spectroscopy, swelling behavior, weight loss (degradation), and pH variations.

Results: FTIR confirmed successful incorporation of the nanoparticles within the hydrogel matrix. The samples demonstrated initial pH reduction followed by gradual alkalization, indicating buffering potential. Swelling and degradation assays showed controlled fluid absorption and biodegradable nature, influenced by nanoparticle concentration.

Conclusion: These results suggest the potential of the designed hydrogel as a promising scaffold for drug delivery system in brain tumor therapy.

Keywords: Glioblastoma, Hydrogel, Zinc Oxide Nanoparticles, Drug Delivery System

Ps-107: Hypoxia-Mimetic Lactic Acid Preconditioning Augments Pro-Angiogenic Activity of MSC Secretomes in Endothelial Cell Models

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Objective: Cardiovascular diseases remain a primary cause of mortality worldwide, underscoring the need for innovative therapeutic approaches such as therapeutic angiogenesis to restore perfusion in ischemic myocardium. Mesenchymal stem cells (MSCs) are promising candidates for cardiac repair due to their secretion of paracrine factors with pro-angiogenic, anti-apoptotic, and anti-inflammatory effects. Recent evidence suggests that pre-conditioning MSCs can further amplify their reparative properties. This study investigates lactic acid (LA) pre-conditioning as a hypoxia-mimetic intervention—capitalizing on the Warburg effect—to potentiate the angiogenic activity of MSC-derived secretomes. We hypothesized that LA pre-conditioning would significantly enhance the angiogenic potential of MSC secretions.

Materials and Methods: The research was conducted in two phases: (1) identification of the optimal LA concentration for MSC pre-conditioning, and (2) assessment of the effects of LA-preconditioned MSC conditioned medium (MSC-LA) on the proliferation and migration of human umbilical vein endothelial cells (HUVECs) in vitro.

Results: MSCs preconditioned with 10 mM LA exhibited increased metabolic activity. Furthermore, HUVECs exposed to MSC-LA showed significantly elevated proliferation and migration rates compared to untreated controls ($p < 0.05$).

Conclusion: Lactic acid pre-conditioning effectively enhances the in vitro angiogenic potential of MSC secretions, suggesting a promising strategy for improving stem cell-based therapies for cardiovascular disease.

Keywords: Mesenchymal stem cells, lactic acid pre-conditioning, hypoxia-mimetic, angiogenesis, cardiovascular repair

Ps-108: Assessment of Protein Content in Conditioned Media

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Objective: Conditioned media is rather a novel cell-based approach to obtain benefits of the cells as a treatment. Storing the media, on the other hand rises a challenge. Lyophilization is widely used to preserve bioactive components in conditioned media, ensuring long-term stability and ease of storage. However, the protein content within the media plays a crucial role in determining post-lyophilization structural integrity and bioactivity. The lyophilization process must be designed in a standard way to keep the conditioned media in its defined and characterized state.

Materials and Methods: For this matter, conditioned media of placenta-derived stromal cells was commercially bought, filtered and centrifuged to remove cellular debris. Lyophilization process, assisting pressure and thermal changes, will leave a freeze-dried powder stored in -21 °C. Protein concentrations were quantified using a Bradford assay. Rehydrating the lyophilized conditioned media was done with complete DMEM/F12 Media containing 10% FBS and 1% each non-essential amino acids, pen strep and Glutamax. To find an optimum dose, human dermal fibroblasts cellular function and morphology was assed in different concentrations of conditioned media, 100%, 50%, 25% and 12.5%.

Results: Post-lyophilization analyses included total protein concentration, solubility and whether cellular functions were affected in contact with the rehydrated conditioned media. Dose finding of this test indicates that using 1:1 ratio (rehydrating 1 unit of conditioned media to 1 unit respectively) might be toxic in protein quality of quantity for the incubated human dermal fibroblast cells.

Conclusion: In conclusion, total protein concentration and quality is a crucial factor to take into consideration while assessing the bioactivity of a conditioned media, using precise percentage of FBS as a source of protein and conditioned media for tailored purposes.

Keywords: protein, conditioned media, lyophilization

Ps-109: Modulatory Effects of Human Placenta Extract on Cancerous Phenotype in Hepatocellular Carcinoma Cells

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Objective: Liver Cancer is one of the most significant health concerns globally, and as estimated new cases may exceed 1 million each year by 2025. Hepatocellular carcinoma (HCC) accounts for approximately 90% of all liver cancer cases; however, current treatment modalities remain limited. Recently, advanced studies in regenerative medicine have resulted in the creation of Advanced Therapy Medicinal Products (ATMPs), including tissue-engineered medicinal products. The human Placenta is a rich source of extracellular matrix (ECM) and different biomolecules, particularly known for their anti-inflammatory properties. Therefore, the objective of this study is to make use of decellularized ECM of the human placenta in order to observe its potential impact on the cancerous phenotype of HCC cells.

Materials and Methods: Huh7 cells were treated with human placenta extract (hPE). In order to determine the optimal dosage, cell viability was performed using MTS assay after 24 and 48 hours of treatment. After the identification of the preferable concentration, the effects of human placenta extract on cell migration and invasion were assessed using wound healing and transwell assay.

Results: Treatment with hPE suppressed the cancerous traits in Huh7 cell line. A significant reduction in cell viability was observed following the treatment with hPE. Additionally, the extract noticeably reduced the migration and invasion capacities of Huh7 cells.

Conclusion: hPE has demonstrated a promising potential in attenuating cancerous phenotype including cell viability, migration, and invasion. With further studies, hPE may contribute to serve as a potential candidate for combination therapies in HCC.

Keywords: Hepatocellular Carcinoma, Human Placental Biomaterials, Cell Migration, Invasion

Ps-110: Multifunctional Scaffold Based on Polycaprolactone-Gelatin/Fibrin/Bacterial Nanocellulose Containing Hydroxyapatite-Nanorods as A Bone Substitute in Regenerative Dentistry

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Objective: Guided tissue regeneration (GTR) is an approach aimed at regeneration of different tissues in close proximity, while keeping them from intermingling. This method is studied, especially for regenerating periodontal tissues. A key aspect of this strategy is the design of composite scaffolds, where each layer provide differentiation capabilities appropriate to the specific tissue type while preventing the invasion of surrounding and non-target tissues.

Materials and Methods: For obtaining better therapeutic effects, multifunctional composite scaffold containing a three-layered structure designed to promote the regeneration of alveolar bone defects although preventing the penetration of adjacent soft tissue from growing into the bone area.

Results: Two of the layers were made from bacterial cellulose integrated with hydroxyapatite nanorods (HAP-nanorods), (747±11 nm) and Platelet-Rich Fibrin (PRF) to aid in bone regeneration. The third layer is an electrospun nanofibrous polycaprolactone-gelatin membrane (PCL-GEL) serves as a barrier against soft tissue migration. The bacterial cellulose layer provided a suitable three-dimensional substrate (Pore size 250±83 µm and BET surface area 34.60 m²/g) for stem cells to enter this region. Furthermore, the attachment of antibacterial hydroxyapatite nanorods based on iron nanoclusters functioned as an inhibitor of local bacterial infections as well as an osteoinduction stimulator. By adding PRF, which is rich in growth factors, tissue regeneration was greatly expedited. Meanwhile, soft tissue fibroblast migration to the bone area was successfully inhibited by the polycaprolactone-gelatin nanofibrous barrier, which also promoted gingival regeneration at the site of damage.

Conclusion: Overall, this scaffold could play an efficient role in GTR and alveolar bone regeneration and provide good application prospect for bone repair in clinic.

Keywords: GTR, Scaffold, PCL-GEL, Fibrin, Bacterial nanocellulose-HAP

Ps-111: Synergistic Effect of Carboxymethyl Chitosan Hydrogel and Adm-sc-Derived Exosome for Inducing Osteo-Differentiation

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Objective: Bone regeneration, especially in large defects, remains a major clinical challenge due to the insufficiency of natural healing. Exosomes, as extracellular nano-vesicles secreted by mesenchymal stem cells (MSCs), have attracted considerable attention for their regenerative capabilities. The aim of this study is to investigate the effect of adipose-derived MSC exosomes combined with a carboxymethyl chitosan hydrogel on enhancing osteogenic differentiation.

Materials and Methods: Chitosan/carboxymethyl chitosan (CS/CMC) hydrogel morphology was observed by scanning electron microscope (SEM). Human mesenchymal stem cells were isolated from adipose tissue and encapsulated in a CS/CMC hydrogel. Cell viability and proliferation of MSCs were evaluated at 24 and 72 hours using the MTT assay. Osteogenic differentiation was assessed over 14 days using Alizarin Red staining for calcium deposition and immunocytochemistry (ICC) for OSTEONECTIN protein expression.

Results: SEM image illustrated the porous structure. MSCs viability was increased at 24 and 72 hours. Alizarin Red staining confirmed the presence of calcium deposits. ICC analysis dem-

onstrated OSTEONECTIN expression (39.61%).

Conclusion: The addition of adipose-derived MSC exosomes to the CS/CMC hydrogel enhanced cell viability and promoted osteogenic activity. This approach may offer a promising strategy for the development of biocompatible systems in bone tissue engineering.

Keywords: Exosome, Carboxymethyl Chitosan, Adipose-derived Stem Cell, Osteogenesis

Ps-112: In Silico Simulation of Toehold-Mediated Strand Displacement (TMSD) Reactions Using the NUPACK Bioinformatics Tool: Toward Stem Cell Monitoring Applications

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Objective: The analysis and design of RNA and DNA structures are not only essential in molecular biology but also play a crucial role in the development of artificial systems within the field of DNA nanotechnology. DNA nanotechnology is an emerging field that leverages molecular design principles to construct biological circuits, sensors, and computational systems. Among the key mechanisms used in designing such systems are toehold-mediated strand displacement (TMSD) reactions. In this study, the NUPACK bioinformatics software—recognized as one of the main tools for simulating and analyzing DNA secondary structures—was employed.

Materials and Methods: This study focused on the design and simulation of autocatalytic systems based on TMSD within the realm of DNA nanotechnology. The autocatalytic circuit design involved specifying the domains of oligonucleotide strands and constructing hairpin structures (H1, H2, H3, Hp), along with input oligonucleotides and a DNzyme. The reactions were simulated under optimized conditions at 25 °C with defined salt concentrations. The NUPACK platform enabled thermodynamic analysis and behavioral prediction of these systems.

Results: The addition of an input strand to the hairpin structures generated a Y-shaped three-way junction that produced a trigger with a, b, and c domains, capable of re-entering the autocatalytic cycle. The G-quadruplex structure designed was active due to the presence of guanine domains; however, after the TMSD reaction and DNzyme binding, the structure opened and the DNzyme signal was quenched due to the spatial separation of the guanine domains.

Conclusion: Simulations demonstrated the probability of DNA complex formation ranged between 0.994 and 1.000, indicating structural stability and design validity. The use of NUPACK facilitates precise design and efficient optimization of complex strand displacement reactions. This programmable molecular system holds particular promise for stem cell research, where precise detection of biomarkers like microRNAs could enable real-time monitoring of stem cell quality, differentiation status, and therapeutic potential in regenerative medicine applications.

Keywords: DNA nanotechnology, Toehold-mediated strand displacement (TMSD), NUPACK, G-quadruplex DNzyme, Stem cell monitoring

Ps-113: Regeneration of Amputated Mouse Digit Tip Using Bone Marrow-Derived Mesenchymal Stem Cells Induced by CHIR99021

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Objective: Digit tip regeneration remains a significant challenge in regenerative medicine. While stem cell-based therapies have shown promise, their clinical translation is hindered by limited cell proliferation and tissue integration at the amputation site. CHIR99021, a small molecule CHIR99021 known to activate WNT/ β -catenin signaling, has been demonstrated to enhance the proliferation and differentiation of mesenchymal stem cells (MSCs). In this study, we evaluate the regenerative potential of bone marrow-derived MSCs pretreated with CHIR99021 to the repair of amputated mouse digit tips.

Materials and Methods: Human bone marrow-derived MSCs obtained from the Royan Institute were expanded following confirmation of their multipotency through osteogenic, adipogenic, and chondrogenic differentiation assays. The non-regenerating proximal digit amputation model was employed to evaluate regenerative potential. The optimal and safe concentration of CHIR99021 was determined using the MTS assay. MSCs pretreated with CHIR99021 were embedded in a hydrogel matrix and injected into the amputation site 4 days after injury. Tissue regeneration was assessed via macroscopic observation, histological analysis (Hematoxylin & Eosin (H&E) and Masson's Trichrome staining).

Results: The identity of hBM-MSCs was confirmed by their characteristic morphology and their ability to differentiate into osteogenic, adipogenic, and chondrogenic lineages. Histological analysis revealed that the hBM-MSCs/CHIR99021/HG group showed abnormal formation of nail and nail-bed structures, which was not observed in the untreated control group. In contrast, no significant tissue repair was detected in the CHIR99021/HG or hBM-MSCs/HG groups.

Conclusion: hBM-MSCs preconditioned with CHIR99021 represent a promising therapeutic approach for fingertip regeneration. By enhancing stem cell proliferation and differentiation, this small molecule may help overcome current limitations in regenerative medicine and improve outcomes for patients with finger amputations. However, further investigations are required to optimize the approach and validate its efficacy in clinical settings.

Keywords: Mesenchymal Stem Cells, CHIR99021, Digit tip regeneration, WNT signaling pathway

Ps-114: Treatment of Alginate/Gelatin Hydrogel Cultured Human Endothelial Progenitor Cells with Melatonin Promoted Angiogenesis

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Objective: Endothelial progenitor cells (EPCs) are valid cell sources for the induction of angiogenesis in in vitro and in vivo conditions. Several metabolites and compounds can control the function of EPCs via various underlying mechanisms. Melatonin is a hydrophobic hormone with pleiotropic properties in different cell lineages. Here, we aimed to explore the possible stimulatory/inhibitory angiogenesis properties of melatonin on EPCs.

Materials and Methods: EPCs were isolated by Ficoll-Paque gradient centrifugation and characterized using Dil-AC-LDL uptake and western blotting. Alginate/gelatin hydrogel was fabricated using ionic cross-linker 0.2 M CaCl₂. Alginate/gelatin cultured EPCs were incubated with 0.2 M melatonin for 5 days and maturation, migration, and angiogenesis were monitored using western blotting, and PCR array analysis.

Results: Cells showed fibroblast-like morphologies with the ability to internalize Dil-Ac-LDL and express CD133, CD34, VEGFR-2, and Tie-2, indicating a typical EPC phenotype. Data indicated that melatonin can increase the viability of EPCs in a dose-dependent manner. Cultured EPCs on alginate/gelatin revealed no toxicity compared to the control cells expanded on the plastic surface. 5-day exposure of EPCs to melatonin led to the maturation of these cells into endothelial cells indicated with VEGFR-2, VEGF, vWF, and VE-cadherin, and an increase of Ang-1, and Ang-2 ($p < 0.05$). These data coincided with the stimulation of migration capacity in the Transwell insert compared to the non-melatonin-treated group. PCR array indicated the activation of several genes related to cell migration and movement.

Conclusion: We conclude that injection of melatonin-treated EPCs loaded in alginate/gelatin hydrogel exhibited prominent angiogenesis properties with enhanced survival rate and migration capacity.

Keywords: Endothelial Progenitor Cells, Melatonin, Angiogenesis, Alginate/gelatin hydrogel

Ps-115: Efficacy and Predictors of Immunotherapy in Gastric Cancer: A Systematic Review of Recent Evidence

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Objective: Gastric cancer (GC) continues to be a major cause of cancer deaths worldwide. Immunotherapy, especially immune checkpoint inhibitors (ICIs), has emerged as a promising treatment strategy. Despite some success, variability in patient response highlights the need for synthesis of recent evidence on its effectiveness and biomarkers.

Materials and Methods: This systematic research followed PRISMA guidelines. The research team searched PubMed, Scopus, and Web of Science databases for systematic reviews and meta-analyses from 2020 to 2025. The research included studies about GC patients who received immunotherapy treatment with three specific outcome measures: Overall survival (OS), progression-free survival (PFS) and response rates, and biomarkers or predictors of response. The research team analyzed 9 high-quality systematic reviews and meta-analyses.

Results: The first-line treatment of advanced GC with immunotherapy and chemotherapy resulted in substantial OS benefits. The survival benefits of pembrolizumab with chemotherapy exceeded those of chemotherapy alone only in patients with PD-L1 CPS ≥ 10 but not in patients with CPS < 1 . A meta-analysis found that lactate dehydrogenase (LDH) and glycolytic activity independently predicted poor ICI response. The majority of immune-related toxicities were controllable but gastric cancer patients experienced more hematologic side effects than esophageal cancer patients.

Conclusion: The survival benefits of immunotherapy become most pronounced in advanced gastric cancer patients who express high levels of PD-L1. The predictive value of CPS, LDH, and glycolytic phenotype biomarkers helps determine treatment response. The optimal treatment outcomes require biomarker-based selection and the integration of immunotherapy with multimodal treatment approaches. Future research should concentrate on improving biomarker thresholds and creating individualized treatment protocols. The assessment of response durability and late-onset toxicity management requires extended follow-up data.

Keywords: Gastric cancer, Immunotherapy, Immune checkpoint inhibitors, Pembrolizumab, Progression-free survival (PFS)

Ps-116: Engineering CAR-T and TCR-T Cells to Target Glioma Stem Cells: A Systematic Review of Therapeutic Innovations (2020–2025)

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Objective: Glioblastoma (GBM) represents an aggressive brain tumor that originates from glioma stem cells (GSCs) while these cells evade standard treatments and lead to tumor relapse. The targeted therapy of cellular immunotherapy focuses on GSC-specific antigens through CAR-T and TCR-T cells. The engineering strategies work to address the challenges of antigen heterogeneity, immune evasion, and the immunosuppressive nature of the tumor microenvironment (TME).

Materials and Methods: We followed PRISMA guidelines to conduct a systematic review of studies from 2020–2025 that investigated CAR-T and TCR-T cell engineering against GSCs. The inclusion criteria consisted of: (1) Systematic reviews or meta-analyses; (2) Engineered CAR/TCR T cells targeting GSCs; (3) Outcomes on tumor regression, T-cell persistence, and immune escape. Seven studies met inclusion.

Results: CAR-T cells that targeted CD133 as a GSC marker showed limited effectiveness because of antigen heterogeneity and TME suppression. Preclinical models showed that dual-targeted CARs (e.g., CD133+IL13R α 2 and CD70+EGFRvIII) achieved better cytotoxicity and reduced tumor escape. TCR-T cells that targeted HLA-A2-restricted antigens including NY-

ESO-1 and Survivin showed superior tumor penetration and survival rates than CAR-T cells in GBM mouse models. The use of cytokine engineering (e.g., IL-12-secreting CAR-Ts) improved anti-GSC responses and transformed the immunosuppressive environment. TCR-T therapy faces two main limitations which include HLA-restriction and off-target toxicity.

Conclusion: The preclinical data indicates that GSC-targeted CAR-T and TCR-T therapies are promising when dual-antigen targeting and cytokine support are used. The development of T-cell engineering strategies that enhance T-cell survival, broader antigen recognition, and resistance against TME is essential. The clinical application of these therapies will need safer constructs and improved biomarkers for GSC detection.

Keywords: CAR-T Cell Therapy, TCR-T Cell Therapy, Glioblastoma (GBM), Glioma Stem Cells (GSCs), Antigen Heterogeneity

Ps-117: Exploring the Anti-Cancer Effects of Mesenchymal Stem Cell-Derived Exosomes: A Systematic Review

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Objective: Mesenchymal stem cell-derived exosomes (MSC-Exos) have emerged as promising cell-free therapeutic tools in cancer treatment. Compared to direct stem cell transplantation, MSC-Exos offer superior safety, reduced immunogenicity, and eliminate risks associated with uncontrolled cell proliferation. Furthermore, unlike conventional chemotherapeutic agents, MSC-Exos possess intrinsic tumor-targeting capabilities and can deliver functional bioactive molecules—such as miRNAs and proteins—across biological barriers with minimal off-target toxicity. These advantages position MSC-Exos as a minimally invasive and effective strategy in oncological therapy. This systematic review aims to critically evaluate and integrate current preclinical and clinical evidence on the therapeutic potential of MSC-derived exosomes in various cancer types.

Materials and Methods: A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, and Embase up to May 2025. Studies investigating MSC-derived exosomes in cancer models were included. Data were extracted regarding exosome isolation methods, cancer type, molecular mechanisms of action, and therapeutic outcomes.

Results: A total of 87 studies were included, comprising 71 preclinical and 16 clinical or translational studies. MSC-Exos demonstrated significant anti-tumor effects in cancers such as breast, lung, colorectal, and ovarian. These effects were primarily mediated through the delivery of tumor-suppressive miRNAs (e.g., miR-21, miR-124), induction of apoptosis, modulation of the tumor microenvironment, and immune regulation. Several studies also reported enhanced therapeutic efficacy when MSC-Exos were combined with conventional chemotherapy. However, challenges such as variability in exosome isolation protocols and heterogeneity in exosomal content remain critical issues for clinical translation.

Conclusion: MSC-derived exosomes represent a powerful and safe cell-free platform for cancer therapy. Despite their demonstrated efficacy and low toxicity, standardized production meth-

ods and well-designed clinical trials are essential to facilitate their clinical application in oncology.

Keywords: Cancer, Exosome, Mesenchymal Stem Cell

Ps-118: Current Evidence on Cell Therapy Strategies in Acute Myeloid Leukemia: A Systematic Review of Transplant and CAR-Based Approaches (2020–2025)

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Objective: Acute myeloid leukemia (AML) is a hematologic malignancy with high relapse rates even with strong chemotherapy. Recent advances in cellular therapies, including hematopoietic stem cell transplantation (HSCT) and CAR-based immunotherapies, offer potential curative options. This review synthesizes updated evidence on efficacy and prognostic determinants of cell therapy in AML.

Materials and Methods: The research followed PRISMA guidelines on writing systematic review and meta-analysis. The research team searched PubMed, Scopus, and Embase databases for AML studies about HSCT and CAR-based strategies from 2020 to 2025. The inclusion criteria consisted of (1) prospective or retrospective systematic reviews/meta-analyses; (2) adult AML populations; (3) evaluation of outcomes such as relapse-free survival (RFS), overall survival (OS), and treatment-related mortality (TRM). Seven studies met the inclusion criteria for this review.

Results: The cornerstone for curative intent in high-risk AML remains Allogeneic HSCT. A meta-analysis showed that patients who received matched unrelated donor HSCT had better OS compared to those who received chemotherapy alone. The addition of FLT3-inhibitor maintenance therapy after HSCT resulted in lower relapse rates for patients with FLT3-ITD+ AML. CAR-T cell therapy targeting CD33 and CD123 is being evaluated in early-phase studies for relapsed AML but its persistence and efficacy are limited because of low antigen specificity and myelosuppression. The results of comparative analyses indicate that CAR-T shows promise but it has not surpassed HSCT as a treatment for AML.

Conclusion: The field of AML cell therapy continues to develop. The standard treatment for AML patients remains allogeneic HSCT while molecular risk assessment guides treatment decisions. CAR-T cell therapy demonstrates promise but its effectiveness is restricted by its inability to target antigens and its short-term durability. Future trials are critical for AML focusing on dual-antigen targeting and safer constructs.

Keywords: Acute Myeloid Leukemia (AML), Allogeneic Hematopoietic Stem Cell Transplantation (HSCT), CAR-T Cell Therapy, FLT3 Inhibitor, Relapse-Free Survival (RFS)

Ps-119: DROSHA regulatory protein indicate significant changes in Substantia Nigra region of Parkinson's Disease

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Objective: Parkinson's disease (PD) is a chronic and progres-

sive neurodegenerative disorder characterized by impaired motor function, primarily resulting from the degeneration of dopaminergic neurons in the brain. Although significant research has been conducted, the molecular basis of PD remains poorly understood.

Materials and Methods: In this study, we performed a comprehensive transcriptomic analysis to identify differentially expressed genes (DEGs) in individuals with Parkinson's disease compared to healthy controls. Using dataset GSE150696 from the Gene Expression Omnibus (GEO), we identified a total of 1,455 DEGs—674 of which were upregulated and 781 down-regulated.

Results: Through protein-protein interaction (PPI) network construction using the STRING database and Cytoscape software, we identified nine key upstream regulators potentially implicated in the disease's pathogenesis. Among these, DROSHA emerged as a previously unreported regulatory protein in the context of PD, suggesting its potential as a novel therapeutic target.

Conclusion: These insights contribute to a deeper understanding of the molecular framework of Parkinson's disease and may pave the way for the development of more precise therapeutic interventions. Future research focusing on genetic profiling and biomarker discovery could lead to improved strategies for diagnosis and treatment.

Keywords: Parkinson's Disease, Gene Expression, Microarrays, Bioinformatics, Upstream analysis

Ps-120: Sustained Release of Parathyroid Hormone (1-34) from Covalently Functionalized Polylactic Acid Scaffolds for Enhanced Bone Regeneration

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Objective: Polylactic acid (PLA) is a widely utilized polymer for bone scaffold fabrication but possesses limitations such as hydrophobicity and bioinertness, hindering cell adhesion and tissue integration. Parathyroid hormone fragment 1-34 (PTH1-34) is an FDA-approved osteoanabolic peptide that enhances osteoblast activity. This study aimed to improve PLA scaffold properties by covalently immobilizing PTH1-34 onto their surface.

Materials and Methods: PLA scaffolds, fabricated by salt leaching and characterized (SEM, porosity), underwent surface activation. Amine groups were generated using ethylenediamine solution, and carboxyl groups via NaOH treatment. Functional group quantification was performed using Toluidine Blue and Coomassie Brilliant Blue and employed for optimization of treatment times. PTH1-34 was conjugated to activated surfaces using EDC/NHS chemistry. Attenuated Total Reflectance Infrared (ATR-IR) spectroscopy monitored chemical changes, and PTH1-34 release profiles were determined.

Results: Scaffolds exhibited interconnected pores (200-600 µm) and high porosity (~79%). Optimal surface activation times for aminolysis (30 min) and hydrolysis (60 min) were established. ATR-IR spectroscopy confirmed successful surface amination, hydrolysis, and subsequent PTH1-34 conjugation, evidenced by characteristic spectral changes indicating amide

bond formation. PTH1-34 release from untreated and aminated scaffolds was rapid, while carboxylated scaffolds with conjugated PTH1-34 showed a sustained and steady release.

Conclusion: PTH1-34 was successfully immobilized on PLA scaffolds, particularly via surface-generated carboxyl groups. This covalent conjugation strategy resulted in a sustained release profile for PTH1-34, indicating its potential for enhancing the osteoinductive properties of PLA-based bone scaffolds.

Keywords: Tissue Engineering Scaffold, Parathyroid Hormone, Poly Lactic Acid, Covalent Conjugation

Ps-121: Activation of the Wnt signaling Pathway Promotes Angiogenic Potential in Human Endothelial Progenitor Cells

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Objective: Endothelial progenitor cells (EPCs) are valid stem cell source for the induction of angiogenesis in numerous ischemic tissues. Targeting the signaling pathways involved in the transcriptional regulation and post-translational modifications of pro-angiogenic factors may enhance therapeutic outcomes. This study aimed to investigate the effects of activating or inhibiting the Wnt signaling pathway on EPC function and angiogenic potential.

Materials and Methods: Endothelial progenitor cells (EPCs) were isolated from human bone marrow samples using Ficoll-Paque and cultured in DMEM/F12 medium supplemented with EGM-2. Following characterization, EPCs were treated with a Wnt agonist and antagonist. Cell viability upon exposure to the tested doses was evaluated using the MTT assay. The migration capacity of EPCs were evaluated using Transwell Inserts after 5 days.

Results: The isolated cells expressed surface markers CD133, CD34, VEGFR-2, and Tie-2, and were capable of uptaking Dil-Ac-LDL, confirming their stemness and differentiation toward the endothelial lineage. MTT assay results demonstrated that the tested doses of Wnt agonist and antagonist were non-toxic to EPCs. Morphologically, EPCs in the control and antagonist-treated groups maintained a typical spindle-shaped appearance, while cells in the Wnt agonist group exhibited notable morphological changes. Moreover, activation of the Wnt signaling pathway significantly enhanced EPC migration compared to control and antagonist-treated groups.

Conclusion: Activation of the Wnt signaling pathway promotes the morphological transformation and migratory capacity of human EPCs under in vitro conditions. These findings suggest that Wnt pathway activation may accelerate the maturation of EPCs into functional endothelial cells, thereby improving their

angiogenic potential.

Keywords: Human Endothelial Progenitor Cells, Wnt signaling pathway, cellular Morphology, Cell migration

Ps-122: Synergistic Effects of Wharton's Jelly MSC-Conditioned Medium and Microbial Exopolysaccharide on Diabetic Wound Healing: In Vitro and In Vivo Evaluations

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Objective: Chronic diabetic wounds are a major clinical challenge, often resistant to conventional therapies. In this study, we evaluated the healing potential of a novel combination therapy consisting of exopolysaccharide derived from *Rhodotorula mucilaginosa* sp. GUMS16 (EPS-GUMS16) and conditioned medium derived from Wharton's jelly mesenchymal stem cells (WJ-MSCs-CM).

Materials and Methods: In vitro, MTT and scratch assays were performed to evaluate the effects of EPS, WJ-MSCs-CM, and their combination on the proliferation and migration of human dermal fibroblasts (HFF) and endothelial cells (HUVECs). In vivo, full-thickness excisional wounds were created on streptozotocin-induced diabetic rats. Treatments were administered topically and via periwound injection. Wound healing was assessed histologically on days 7 and 14 post-injury using hematoxylin-eosin (H&E) and Masson's trichrome staining.

Results: The combination of EPS-GUMS16 and WJ-MSCs-CM significantly enhanced fibroblast proliferation and migration in vitro, compared to each agent alone. Histological analysis showed that the combined treatment accelerated re-epithelialization, improved granulation tissue organization, and reduced inflammatory infiltration and edema in diabetic wounds. These findings suggest a synergistic effect of EPS and WJ-MSCs-CM on key cellular and tissue-level processes involved in wound repair.

Conclusion: The EPS-GUMS16/WJ-MSCs-CM combination therapy demonstrates promising regenerative effects in diabetic wound healing, and represents a potential cell-free therapeutic approach for chronic skin injuries.

Keywords: Diabetic wound healing, Exopolysaccharide, Wharton's jelly mesenchymal stem cells

Ps-123: Three Dimensional Bioprinting of Full-Scale, Patient-Specific Meniscus Constructs Using Crosslinker-Free Silk Fibroin Bioink

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Objective: Knee meniscus remains a major challenge due to its unique structure, load-bearing function, and need for both

biological and mechanical compatibility. Success in this area depends heavily on the development of a bioink that is strong, printable, cytocompatible, and safe for clinical translation.

Materials and Methods: A three-dimensional meniscus model was reconstructed from patient-specific MRI data using Mimics software and served as the design 3D model for bioprinting. The bioink was formulated using silk fibroin and polyethylene glycol (PEG), forming a crosslinker-free hydrogel system. This combination enabled gelation without the use of cytotoxic chemical agents while maintaining printability and biocompatibility. This study represents the first reported application of a silk fibroin-PEG bioink in the field of meniscus tissue engineering.

Results: Gelation was induced using polyethylene glycol (PEG), eliminating the need for toxic chemical crosslinkers. This allowed direct encapsulation and bioprinting of chondrocyte cells (C28/I2 line), maintaining over 92% cell viability after 24 hours, and ensuring minimal cell damage during extrusion. Rheological characterization revealed pronounced shear-thinning behavior, with viscosity decreasing from ~1100 cP to ~200 cP as shear rate increased from 100 to 1000 s⁻¹. The gel also exhibited a stable elastic profile with a storage modulus (G') of approximately 8000 Pa, confirming its structural consistency and suitability for extrusion-based printing. Printed constructs exhibited a compressive strength of 52 ± 3 kPa, and cyclic compression tests over 20 cycles at 10% strain showed minimal mechanical degradation.

Conclusion: Altogether, this bioink offers a safe, printable, and mechanically sound solution for building personalized meniscus scaffolds—bringing us closer to clinically viable bioprinting for orthopedic repair.

Keywords: bioprinting, self-standing bioink, meniscus tissue engineering, mimics software, silk fibroin

Ps-124: Improvement of Clinical Symptoms Following Transplantation of Cardiomyocyte-like Cells Loaded on Hydrogel Scaffold in the Model of Chronic Myocardial Infarction in Sheep

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Objective: Background: Myocardial infarction (MI) is the permanent and irreversible cell death of a portion of the heart muscle. Due to the limited ability of the heart to regenerate itself, the damaged portion of the myocardium cannot be replaced by conventional therapies. Therefore, there is a need for new solu-

tions to regenerate or replace the damaged heart tissue. **Objective:** The aim of the study was to evaluate the changes in clinical symptoms following the transplantation of cardiomyocyte-like cells differentiated from adipose tissue mesenchymal stem cells and loaded onto a hydrogel scaffold (CLC+Hydrogel) in an experimental model of chronic MI in sheep.

Materials and Methods: **Materials and Methods:** In this study, 6 male sheep were randomly divided into the treatment and control groups. Adipose tissue mesenchymal stem cells were differentiated into the cardiomyocyte-like cells by azacytidine-5, fibroblast growth factor-2, and Vitamin-C. Also, a hydrogel scaffold was made from the combination of chitosan and polyvinyl alcohol. MI was created surgically by ligating one of the branches of the left anterior descending (LAD) artery in sheep of both groups. After 6 weeks, the sheep were again operated and CLC+Hydrogel was injected around the infarcted areas in the treatment group and PBS in the control group. In both groups, the clinical symptoms were recorded one day before MI and 6 weeks after MI (the day before transplantation) and on days 1, 7, 30, and 60 after transplantation.

Results: **Results:** The clinical findings showed that chronic MI was induced in sheep six weeks after the LAD artery ligation. As an increase in heart rate (HR), abnormal heart sounds, irregular heart rhythm and a decrease in heart beat intensity were evident compared to before surgery. However, after CLC+Hydrogel transplantation, HR, sounds, rhythm and intensity returned to pre-surgery status over time and the heart condition improved compared to the control group. After MI induction and before transplantation, in sheep of both groups, abnormal lung sounds and respiratory rate increased, mucous membranes (gums and conjunctiva) showed changes towards hyperemia, appetite decreased and sheep were depressed, but in the treatment group after CLC+Hydrogel transplantation, the condition of the lungs, mucous membranes, appetite and physical situation of the sheep improved on different days compared to the control group. While, in the control group, the clinical signs were abnormal until the end of the study.

Conclusion: **Conclusion:** The results obtained from clinical symptoms in the treatment group and its comparison with the control group indicated the positive effects of CLC+Hydrogel transplantation on the improvement of chronic MI in sheep.

Keywords: Chronic Myocardial Infarction, Cardiomyocyte-Like Cells, Hydrogel Scaffold, Sheep

Ps-125: Human Platelet Lysate Improves the Persistence and Memory Phenotype of CAR T cells

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Objective: Chimeric antigen receptor T (CAR T) cell therapy has challenges such as disease relapse, which can be caused by the cells' low persistence. Studies have shown that a less differentiated phenotype can reduce this possibility. Changing culture media can help us find suitable culture medium for GMP-grade productions with a less differentiated phenotype. In this study, we compared the differences between CAR T cells produced in FBS and HPL-containing media.

Materials and Methods: We studied differences in CAR T

cells produced in FBS and HPL supplements by evaluating transduction efficiency with CD3 and anti-CD19-CAR markers. Also, to characterize, we examined the memory phenotype with CD3, CCR7, and CD45RA markers; cytotoxicity with the 7AAD and CD3 markers; and exhaustion with the PD-1 and TIM3 markers using flow cytometry.

Results: In the transduction phase, a significant difference was observed between FBS-CAR T and HPL-CAR T, with the percentage of FBS-CAR T being higher than HPL-CAR T. Also, we observed a higher level of more differentiated cells in FBS-CAR T. We did not observe any difference in cytotoxicity between groups, but higher proliferation was observed in HPL-CAR T. Finally, the assessments showed that exhaustion occurred earlier in the FBS-CAR T.

Conclusion: The results showed that FBS-CAR T had less persistence than HPL-CAR T due to a higher percentage of a more differentiated phenotype and also exhausted earlier. Although FBS-CAR T had a higher transduction rate, other advantages of HPL, such as the xeno-free nature of HPL, make it superior to FBS.

Keywords: CAR T cells, Memory phenotype, Fetal bovine serum (FBS), human platelet lysate (HPL), Persistence

Ps-126: Engineering Dual-Targeted Chitosan Nanoparticles for Glioblastoma: Overcoming Brain Barriers and Protein Corona Challenges

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Objective: Glioblastoma (GBM) is a highly aggressive brain tumor with poor prognosis due to the limitations of the blood-brain barrier (BBB) and the blood-brain tumor barrier (BBTB), which restrict effective chemodrugs delivery into the brain parenchyma. Furthermore, the formation of a protein corona (PC) around nanoparticles (NPs) in biological fluids can hinder targeting and lead to off-target accumulation. This study aims to design a dual-targeted nanoparticle system capable of crossing brain barriers while addressing PC-related challenges.

Materials and Methods: Chitosan nanoparticles were surface-modified with D8 and RI-VAP peptides to facilitate BBB penetration and glioma targeting, respectively. Cyclophosphamide was loaded as a model chemotherapeutic agent. NPs were characterized by dynamic light scattering (DLS), scanning electron microscopy (SEM), and zeta potential. PC formation was assessed, and different ligand ratios were optimized to minimize undesired protein adsorption. In vivo BBB and BBTB penetration was evaluated in an orthotopic C6 glioma rat model using fluorescence imaging and histological analysis.

Results: The dual-modified nanoparticles demonstrated favorable physicochemical properties and stability. Optimized ligand presentation reduced nonspecific protein adsorption and preserved targeting efficacy. In vivo, the engineered NPs effectively crossed both BBB and BBTB, accumulating predominantly in tumor site. Reduced off-target organ accumulation confirmed the role of controlled PC formation in enhancing specificity.

Conclusion: This study presents a rationally designed dual-targeted nanoparticle platform that overcomes major biological barriers in glioblastoma therapy. By addressing both brain barrier penetration and protein corona interference, this system improves targeted delivery and holds promise for future clinical

application in central nervous system tumors.

Keywords: Glioblastoma, Blood-Brain Barrier, Blood-Brain Tumor Barrier, Dual-Targeted Chitosan Nanoparticles, Protein Corona

Ps-127: Human Adipose Tissue-Derived Mesenchymal Stem Cells That Grow into Insulin-producing cells Exhibit Pancreatic Beta Cell-Specific Markers

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Objective: The presence of undifferentiated cells in artificial insulin-producing cells (IPCs) increases the chance of tumor formation. This in vitro study aimed to examine the expression of specific markers of pancreatic β cells by IPCs produced from human adipose tissue-derived mesenchymal stem cells (hADSCs) differentiation.

Materials and Methods: hADSCs were transformed into IPCs by administering insulin-transferrin, selenium (ITS), and nicotinamide in a 14-day differentiation protocol. The cells were transfected with 20 μ g of pure Pdx1-pIRES recombinant vector on the tenth day of differentiation. The successful transfection was confirmed by Pdx1 overexpression and GFP fluorescence activity. The differentiated cells' capacity to release C-peptide was used to evaluate their functionality. Gene expression was assessed using real-time PCR. Meanwhile, protein expression was investigated using western blotting.

Results: The transfected cells exhibited fluorescence activity and Pdx1 overexpression. The differentiated IPCs were able to secrete C-peptide. The expression of stem cell-specific markers Oct4 and Nanog was considerably lower in artificial IPCs ($P < 0.0001$ and $P = 0.0021$, respectively). However, the differentiation process caused a substantial increase in tPA expression as a stem cell differentiation marker ($P = 0.0016$). Differentiated cells showed significantly higher levels of MMP-2 and CD24, two newly generated beta cell-related proteins ($P = 0.0006$, and $P = 0.0032$, respectively).

Conclusion: The differentiation technique used in this work produced functional beta-like cells devoid of typical markers of stem cells. The synthetic IPCs displayed characteristics of newly generated β -like cells.

Keywords: human adipose tissue-derived mesenchymal stem cells, artificial insulin-producing cells, differentiation, pancreatic β cells

Ps-128: The Differentiation of hADSCs Into Artificial IPCs Has No Tumorigenic Consequences In Vitro

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Objective: This study examined the *in vitro* tumorigenic potential of IPCs produced by the differentiation of human adipose tissue-derived mesenchymal stem cells (hADSCs).

Materials and Methods: hADSCs were differentiated into IPCs using insulin-transferrin, selenium (ITS), and nicotinamide in a 14-day differentiation protocol. The cells were transfected with 20 µg of pure Pdx1-pIRES recombinant vector on day 10 of differentiation. The successful transfection was confirmed by Pdx1 overexpression and GFP fluorescence activity. The differentiated cells' capacity to release insulin and glucose-dependent C-peptide was used to evaluate their functionality. Gene expression was assessed using real-time PCR, and protein expression was investigated using western blotting.

Results: The transfected cells exhibited fluorescence activity and Pdx1 overexpression. The differentiated IPCs were able to induce glucose-dependent insulin secretion. The differentiated IPCs expressed much lower c-MYC expression compared to undifferentiated hADSCs ($P = 0.0003$). There was a significant elevation in P16 and P21 expression ($P = 0.0045$ and $P = 0.0061$, respectively).

Conclusion: The artificial IPCs showed no signs of expressing tumor-associated markers. The findings imply that the artificial IPC cells lack tumor characteristics *in vitro*.

Keywords: human adipose tissue-derived mesenchymal stem cells, artificial insulin-producing cells, differentiation, tumor

Ps-129: Comparison of Drug Loading in Extracellular Vesicles Derived from Different Chemically Treated Milk

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Objective: As a widely available, safe, and cost-effective source of extracellular vesicles (EVs), milk-derived EVs (miEVs) have recently been introduced as promising drug carriers. The isolation of high-purity miEVs is a crucial step in this application. To achieve this, milk is often treated with EDTA or sodium citrate (SC). However, to the best of our knowledge, no study has compared drug loading in miEVs from EDTA- or SC-treated milk, which was the aim of our study.

Materials and Methods: Here, following the treatment of bovine milk with EDTA or SC, miEVs were isolated using differential ultracentrifugation and characterized using scanning electron microscopy (SEM), dynamic light scattering (DLS), and immunoblotting. Using the incubation method, sorafenib (SOR), an anticancer chemotherapeutic drug, was loaded into miEVs, and drug encapsulation efficiency (EE%) was assessed via spectrophotometry.

Results: miEVs from EDTA- or SC-treated milk were positive for EV-specific markers, CD63 and TSG101, and had a size of <200 nm. Moreover, they exhibited a spherical morphology with intact membranes. Using a fixed SOR:miEVs ratio for comparison, no significant difference in SOR EE% was detected between miEVs from EDTA- or SC-treated milk.

Conclusion: These findings suggest that both EDTA and SC treatment methods yield miEVs with similar drug-loading capacities, providing flexibility in EV isolation protocols for drug delivery applications.

Keywords: Milk derived extracellular vesicle, Exosome, Drug loading, Drug delivery

Ps-130: Isolation and Characterization of Large RBC-Derived Extracellular Vesicles

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Objective: Extracellular vesicles (EVs) are a heterogeneous population of bilayer membrane-enclosed structures released by all cells. Red blood cell (RBC)-derived EVs play critical roles in immunomodulation and nitric oxide homeostasis. In addition, they have been introduced as promising drug carriers. However, most studies on RBC-derived EVs (RBCEVs) have focused on small EVs, while large EVs remain underexplored. Our study aimed to address this gap.

Materials and Methods: Here, group O-negative leukodepleted packed RBCs from healthy donors were treated with Ca²⁺ ionophore to stimulate EV release. Following RBC and cell debris depletion, large RBCEVs were isolated via low-speed centrifugation. The isolated EVs were quantified based on total protein, and their size distribution, polydispersity index (PDI), and zeta potential were examined using dynamic light scattering (DLS). Furthermore, the presence of EV-associated markers CD81 and TSG101 was analyzed by immunoblotting.

Results: The isolated EVs had a concentration of 9.12 mg/250 mL of packed RBCs, a size of 201 nm, and a PDI of 0.03. Their zeta potential was -29.5 mV, and they were positive for CD81 and TSG101. This is the first study to successfully isolate large RBCEVs following low-speed centrifugation, which were lost in previous studies using differential centrifugation.

Conclusion: Since large RBCEVs offer a more feasible and cost-effective subpopulation for isolation compared to small RBCEVs, the findings of this study may be crucial for future RBCEVs biomedical applications.

Keywords: Extracellular vesicle, Exosome, Red blood cell, Isolation

Ps-131: Recent Updates on Extracellular Vesicle Application in Infarct Condition

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Objective: In recent years, the clinical setting has witnessed the emergence of *de novo* therapeutic modalities with higher regenerative outcomes compared to the conventional medications. Of these approaches, extracellular vesicles (EVs) from different sources have revolutionized the human medicine to al-

leviate the pathologies. Clinical manifestations have confirmed the increase of infarct patients due to the life style changes. The increase of scar tissue and aberrant remodeling contribute to loss of cardiac tissue function and outputs. Due to unique physiochemical properties of cardiac tissue, the direct application of stem cells has been limited. Therefore, exosomes (Exos) are alternative therapeutic bullets harboring signaling molecules with few side effects can regulate the dynamic growth of cardiomyocytes and reduce the injured cardiac cells.

Materials and Methods: Here, in this systematic review we explored the recent data associated with the application of exosomes in patients with myocardial infarction.

Results: Data revealed the improvement of heart function parameters and reduction of pathological changes in the myocardium with concomitant angiogenesis potential.

Conclusion: Taken together, exosomes can be used as alternative therapeutics in infarct individuals with possibility to be used as alternative modalities in the clinical setting.

Keywords: Myocardial infarction, Exosomes, Cardiac function, Clinical Trials, Angiogenesis

Ps-132: Design and Fabrication of Three-layer Oxygen Generator Electrospun Scaffold to Enhance Biological Properties of Skin Wound Dressing

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Objective: As the largest and outermost organ of the body, the skin is highly susceptible to various injuries, which can lead to the loss of its physiological and protective functions, ultimately resulting in wound formation. Skin wound healing remains one of the major challenges in regenerative medicine, particularly in chronic wounds, where insufficient oxygen supply can significantly impair the healing process. The use of tissue engineering and the fabrication of electrospun scaffolds have emerged as cost-effective and efficient approaches for creating micro- to nano-fibrous structures, which has led to a major revolution in the field of wound dressings.

Materials and Methods: In this study, a scaffold was designed using a combination of natural and synthetic polymers along with human amniotic membrane powder, in which both bioactive factors and an oxygen-releasing agent are simultaneously incorporated. The scaffold was characterized using Fourier Transform Infrared (FTIR), Scanning Electron Microscopy (SEM), and tensile. The surface hydrophilicity was evaluated using the contact angle test. The 3- (4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay and DAPI staining were used to assess the in vitro biocompatibility of the scaffold.

Results: The experimental results showed that this 3-layer electrospun scaffold containing oxygen generation could efficiently produce oxygen. Fibroblast cell culture on the scaffolds revealed high cell viability, minimal cytotoxicity, and enhanced cell migration, influenced by the release profile of bioactive proteins and oxygen. Therefore, the findings of this study support the simultaneous use of bioactive compounds and oxygen-releasing agents as an effective approach to accelerate skin regeneration.

Conclusion: Accordingly, the designed multilayer scaffold is proposed as a promising candidate for application in skin tissue engineering.

Keywords: skin tissue engineering, hypoxia, oxygen-generating scaffold

Ps-133: Fabrication And Characterization of Poly L-Lysine/Hyaluronic Acid Polyplexes For Gene Delivery Applications

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Objective: The development of tissue malfunctions due to disease or injury has accelerated the growth of the regenerative medicine field, encouraging the advancement of gene therapy. Among positively charged carriers, polyplexes as interpolyelectrolyte complexes form through electrostatic interactions. Poly-L-lysine (PLL) is a safe, stable, and water-soluble polymer, making it useful in gene delivery. Likewise, hyaluronic acid (HA) demonstrates good biocompatibility and targeted delivery in gene delivery. The polyplexes based on PLL and HA provide a suitable carrier for ribonucleoprotein (RNP) delivery, with ideal characteristics for gene therapy.

Materials and Methods: PLL and HA were dissolved. Then, the complexes at different ratios were prepared, followed by dropping HA into the PLL medium using the electrospraying method. Two different concentrations of PLL were introduced to investigate cell viability and the effect of PLL concentration on condensation capacity. Finally, the polyplexes were characterized by dynamic light scattering (DLS), zeta potential, energy dispersive X-ray spectroscopy (EDX), and MTT assay.

Results: The DLS results for PLL /HA polyelectrolyte reveal the nanoparticle size of approximately 61 nm. The size of the higher concentration of PLL is significantly lower. Zeta potential showed a net positive charge on the surface of particles, facilitating the cellular uptake. The EDX results confirm the presence of Na, O, and P, verifying the required complex formation. The MTT assay demonstrated good cell viability. As the PLL concentration increases, cytotoxicity decreases, indicating a concentration-dependent cytotoxicity effect.

Conclusion: The polyplexes are formed through the interaction of oppositely charged polymers. The PLL/HA polyelectrolyte complexes show promising capability for gene delivery due to their size and desired surface charge. Since HA showed negligible cytotoxicity suggests a good biocompatible agent for gene delivery. To conclude, the tunable properties of polyplexes make them a favorable vector for medical applications.

Keywords: Polyplexes, Cationic Polymers, Poly L-Lysine, Hyaluronic Acid, Gene Therapy

Ps-134: Computational Modeling of Neural Stem Cell Differentiation Pathways Using Single-Cell Data Ans Machine Learning Algorithms

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Objective: Understanding the differentiation mechanisms of Neural Stem Cells (NSCs) is fundamental for developing effective strategies in treating neurodegenerative disorders and advancing neural tissue engineering. The advent of single-cell RNA sequencing (scRNA-seq) enables the simultaneous profiling of thousands of individual cells across various differentiation stages. However, analyzing and interpreting the resulting high-dimensional data necessitate advanced computational approaches. This study proposes an integrated framework combining systems biology and machine learning to reconstruct the dynamic trajectories of NSC differentiation and predict cell fate based on gene expression patterns.

Materials and Methods: Human NSC scRNA-seq datasets were retrieved from the Gene Expression Omnibus (GEO) and subjected to preprocessing, dimensionality reduction, and clustering. Differentiation pathways and cellular decision networks were reconstructed using trajectory inference algorithms, including Partition-based Graph Abstraction (PAGA) and Monocle3. To predict cell fate based on gene expression profiles, supervised learning models, including Random Forest and Artificial Neural Networks, were trained and validated.

Results: The reconstructed differentiation trajectories aligned well with prior experimental findings, and the trained models accurately distinguished distinct differentiation branches and predicted cellular identity using gene expression signatures. Feature importance analysis and trajectory mapping revealed that key regulatory genes such as SOX2, ASCL1, and NEUROD1 play crucial roles in lineage segregation and cell fate determination.

Conclusion: The proposed framework offers a powerful computational tool for the targeted modeling of NSC differentiation. It also provides a generalizable platform applicable to other stem cell types, offering valuable insights into single-cell-level decision-making processes and contributing to the optimization of differentiation protocols in regenerative medicine.

Keywords: Neural Stem Cells, Single-Cell RNA Sequencing, Trajectory Inference, Cell Fate Prediction, Machine Learning

Ps-135: Targeting Sirtuin 1 And P16ink4a Pathways with MicroRNA-146a-Loaded Exosomes to Prevent Senescence in Human Mesenchymal Stem Cells

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Objective: Cellular senescence in Human Mesenchymal Stem Cells (HMSCs) presents a significant obstacle to the development of effective cell-based therapies in regenerative medicine. This study aimed to explore whether exosomes engineered to deliver MicroRNA-146A could modulate molecular pathways associated with senescence and improve the functional capacity of aging HMSCs.

Materials and Methods: Exosomes were isolated from Wharton's Jelly-derived stem cells using ultracentrifugation and characterized by nanoparticle tracking analysis and Western blotting for CD63 and CD81 markers. MicroRNA-146A was loaded into exosomes via electroporation, and the engineered exosomes were incubated with HMSCs for 48 hours. Gene expression levels of P16INK4A, P21, and SIRTUIN 1 (SIRT1) were quantified using Quantitative Real-Time Polymerase Chain Reaction (QRT-PCR). Senescence-associated beta-galac-

tosidase (SA- β -GAL) staining was used to assess the proportion of senescent cells.

Results: The results demonstrated a significant reduction in P16INK4A and P21 expression, alongside a marked increase in SIRT1 expression in the treated cells compared to untreated controls ($p < 0.01$). Moreover, the percentage of SA- β -GAL-positive cells was significantly decreased, indicating a functional delay in cellular aging.

Conclusion: These findings suggest that MicroRNA-146A-loaded exosomes effectively target key aging-related genes and pathways to mitigate cellular senescence in HMSCs. The exosomal delivery system offers a promising, non-integrative, and biologically compatible approach for rejuvenating stem cells and enhancing their therapeutic efficacy. This strategy may hold considerable potential in future applications of regenerative medicine and age-related disease intervention.

Keywords: Human Mesenchymal Stem Cells, Cellular Senescence, MicroRNA-146A, Exosomes, Regenerative Medicine

Ps-136: Gene Set Enrichment Analysis of Omics Data of Bmmsc-Derived Exosome in Hypoxia Conditions: A Knowledge-Based Approach

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Objective: MSC-derived exosomes have therapeutic potential by delivering anti-tumor agents and regulatory RNAs. Hypoxia can mediate the tumor microenvironment and is involved in the metastasis and progression of tumor cells. Previous research has indicated that hypoxic conditions can provide a better condition for MSC-derived exosomes and aid in their therapeutic potential. This study analyzed GEO data to explore how hypoxia affects mRNA expression in BMMSC-exosomes.

Materials and Methods: At first, GEO was used to examine the RNAseq data of BMMSC-derived exosomes in hypoxia and normoxia conditions to identify all DEGs linked with hypoxia conditions. Thereafter, based on significant genes (p -value ≤ 0.05), a Protein-protein interaction (PPI) network was constructed with STRING at the Cytoscape software for identifying hub genes. Ultimately, enrichment analysis, including Gene Ontology (GO), was used to explore the related biological processes, molecular functions, cellular components, and KEGG pathway analysis for DEGs.

Results: From 15990 genes obtained from GEO-RNAseq for MSC-derived exosome contents in hypoxic conditions rather than normoxic, 967 DEGs were identified, of which 589 genes were up-regulated, and 338 were down-regulated. According to PPI networks, we identified 767 nodes, based on their degree and interaction; 185 of them have more than 10 interactions and node-degree, including CDCA8, PLK1, CCNB1, AURKA, CDC20, BIRC5, BUB1B, FEN1, and TRIM28. Furthermore, the enrichment analysis showed DEGs have the strongest significance in the Assembly of Checkpoint Signaling, Cell cycle, Golgi and mitochondria cellular components, VEGF, Pentose phosphate, FoxO and P53 signalling pathways, and so on.

Conclusion: Our study identified DEGs, hub genes, and key signalling pathways that may be involved in hypoxic conditions. These findings contribute to a better understanding of

cellular survival mechanisms under hypoxia and may aid in identifying potential prognostic and diagnostic biomarkers. Further investigations are warranted to explore the effects of these exosomes on cancer cell lines.

Keywords: Bone Marrow, Mesenchymal Stem Cell, Extracellular Vesicles, Exosome, Hypoxia

Ps-137: Exosome-Derived Non-Coding RNAs: Promising Biomarkers for Diagnosis, Prognosis, and Personalized Therapy in Acute Myeloid Leukemia

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Objective: Acute Myeloid Leukemia (AML) is a complex malignancy requiring advanced diagnostic tools. Exosomes carry non-coding RNAs (ncRNAs) like miRNAs, lncRNAs, and circRNAs, which regulate gene expression and tumor progression. Exosome-derived ncRNAs from AML patients are promising non-invasive biomarkers for diagnosis, disease stratification, and treatment monitoring. They offer potential for improving diagnostic accuracy, predicting therapy responses, and tracking minimal residual disease (MRD). This systematic review explores the role of exosome-derived ncRNAs in AML, focusing on their potential applications in improving diagnostic accuracy, predicting therapeutic responses, and monitoring minimal residual disease (MRD), thereby advancing personalized medicine in AML management.

Materials and Methods: This systematic review examines the role of exosomes in leukemia, focusing on their ncRNA content in relation to potential diagnostic and prognostic biomarkers. A comprehensive search of PubMed, Scopus, Embase, and Web of Science was conducted, according to PRISMA guidelines with keywords such as AML, Acute Myeloid Leukemia, exosome, and tumor-derived exosome. All English original articles without time limitations were included in our studies.

Results: Based on previous clinical studies, several non-coding RNAs derived from exosomes of AML patients, including miR-542, miR-216b, miR-10a-5p, miR-10b, miR-155-5p, miR-100-5p, miR-146b-5p, let-7a-5p, miR-92a, miR-125b, miR-26a-5p, miR-101-3p, miR-21, and SNHG1, were found to be overexpressed and higher in AML patients compared to healthy controls. In contrast, other non-coding RNAs, such as miR-146a, miR-34a, miR-192, miR-23b-5p, miR-339-3p, miR-425-5p, miR-185-5p, miR-443b-3p, miR-199a-5p, miR-451a, miR-151a-3p, LINC00265, LINC00467, and UCA1, were significantly lower in AML patients compared to healthy controls. These non-coding RNAs have been suggested to be useful as predictive and prognostic biomarkers in AML. Additionally, high expression of microRNA-532 has been associated with favorable overall survival in AML patients.

Conclusion: Exosome-derived ncRNAs show promise as non-invasive biomarkers for AML diagnosis, prognosis, and therapy monitoring, advancing personalized medicine and improving clinical outcomes through targeted strategies.

Keywords: Acute myeloid leukemia, ncRNA, Non coding RNA, exosome

Ps-138: Engineering Dual Anti-CD19/CD22 CAR-NK Cells:

A Step Toward Improved Therapeutic Potential

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Objective: Chimeric antigen receptor (CAR)- cells could change the landscape of cell-based therapies in immunotherapy, particularly in the treatment of hematological malignancies. While CAR-T cells targeting different antigens have achieved significant clinical success, their application has been limited by issues such as antigen loss, cytokine release syndrome, and the need for autologous cell sources. These limitations underscore the need for alternative cell platforms with improved safety profiles and accessibility. Natural killer (NK) cells have emerged as a viable alternative to cell engineering due to their intrinsic cytotoxicity and reduced risk of graft-versus-host disease. However, treatment with these cells also suffers from problems such as disease relapse due to factors such as antigen escape. The dual CAR-NK system is intended to provide broader antigen coverage and reduce the incidence of negative antigen relapse, and could be considered as a solution. Given this, and with the aim of increasing the efficiency of CAR-NK-based cell therapy, in this study, we designed and constructed a dual-targeted CAR construct capable of simultaneously recognizing CD19 and CD22 antigens, both of which are commonly expressed on malignant B cells and are involved in immune evasion mechanisms.

Materials and Methods: A CAR construct targeting both CD19 and CD22 antigens was designed and cloned into a lentiviral expression vector. Lentiviral particles were produced in HEK293T cells using standard packaging plasmids. The construct was successfully transduced into cord blood-derived NK cells. Post-transduction, CAR expression on NK cells was assessed by flow cytometry.

Results: Flow cytometric analysis confirmed acceptable surface expression of the CAR construct on NK cells, indicating its potential to recognize both CD19 and CD22 antigens.

Conclusion: These initial results could demonstrate the feasibility of generating dual CAR-NK cells, which will provide the basis for future functional evaluations aimed at improving the efficacy and sustainability of CAR-based immunotherapies.

Keywords: Immunotherapy, CAR-NK cells, Dual-targeted CAR, anti- CD19/CD22 CAR

Ps-139: Assessment of Fenofibrate's Cytotoxic Impact on Adipose Tissue-Derived Mesenchymal Stem Cells

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Objective: Mesenchymal stem cells (MSCs), particularly those derived from adipose tissue, are of considerable interest in regenerative medicine due to their self-renewal capacity, secretion of bioactive substances, and low immunogenicity, especially when sourced autologously. To enhance the therapeutic potential of these cells, various strategies, including pharmacological preconditioning, have been investigated. This study aimed to examine the effects of fenofibrate- a PPAR- α agonist recognized for its antioxidant, anti-inflammatory, and neuro-

protective properties- on adipose-derived MSCs to augment their secretory functions through pharmacological and cellular engineering techniques.

Materials and Methods: MSCs were isolated from the adipose tissue of adult male rats. Following expansion to the second passage, the cells were exposed to different concentrations of fenofibrate for 48 and 72 hours to assess potential cytotoxicity. Cell viability was determined using the MTT assay.

Results: The MTT assay indicated that after 48 hours of fenofibrate treatment, no cytotoxic effects were observed, and cell viability remained high across all concentrations tested. However, at the 72 hour interval, a dose-dependent decrease in viability was observed, particularly at concentrations of 150 μ M and above. Consequently, 150 μ M was identified as the threshold concentration that induced cellular changes while maintaining an acceptable level of viability.

Conclusion: The findings demonstrate that fenofibrate exerts a time and dose-dependent effect on adipose derived MSCs. Prolonged exposure to the drug resulted in reduced cell viability, suggesting the activation of specific cellular pathways in response to the treatment, while overall cell survival remained within a practical range. These results support the potential application of fenofibrate as a preconditioning agent to modulate MSC behavior without inducing excessive cytotoxicity.

Keywords: Fenofibrate, MTT assay, MSCs, Cell Viability

Ps-140: Design and Fabrication of 3D Printed Polyacrylonitrile/Nanoclay Scaffold for Bone Tissue Engineering

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Objective: Bone injuries are one of the challenges of medical science, which impose many socio-economic consequences on the individual, society, and governments. Regenerative medicine introduces new approaches to improve irreparable bone injury by using tissue engineering and cell therapy methods. 3D printing technology, as a modern and effective technique in designing 3D scaffolds, can produce the morphological structure of human body tissues in a personalized manner.

Materials and Methods: Considering the two polymer and mineral phases of bone, bioceramics are typically used in the mineral phase, and natural or synthetic polymers are used in the polymer phase. In recent years, synthetic polymer scaffolds made of polyacrylonitrile (PAN) have attracted much attention due to their biocompatibility, biodegradability, and high differentiation potential. Clay nanoparticles are silicate particles that have been widely used in tissue engineering due to their ease of fabrication, economic cost, biocompatibility, and high mechanical properties. In addition, adipose-derived mesenchymal stem cells (AD-MSCs) are used in various fields of tissue engineering. Multipotentiality, relative abundance, better control of differentiation are several advantages of these cells rather than other cells. In the present study, optimized scaffolds made of PAN and different percentages of nanoclay were fabricated through 3D printing technology that can induce osteogenic differentiation of AD-MSCs. At first, their structures were assessed through some characterization tests like SEM, FTIR, tensile test and contact angle test for evaluating surface hydrophilicity. After isolation of AD-MSCs, the cell attachment and biocompatibility were determined. Then, osteogenic differentiation-related

markers like ALP and calcium content were studied

Results: The results showed that the addition of nanoclay could enhance the properties of PAN-based scaffolds, such as surface charge, hydrophilicity, roughness, and degradation, as well as osteogenic differentiation of cells.

Conclusion: The nanoClay-PAN scaffolds are suggested as a suitable option for better attachment, proliferation, and differentiation of MSCs

Keywords: tissue engineering, polyacrylonitrile, nanoclay, osteogenic differentiation, 3D printing

Ps-141: Intervertebral Disc Tissue Engineering Using Poly-lactic Acid Nanocomposite and Human Costal Cartilage

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Objective: Intervertebral disc (IVD) degeneration is a principal contributor to chronic spinal pain and significantly impairs patients quality of life. Due to the limitations inherent in conventional treatments, tissue engineering has emerged as a promising strategy for the restoration of disc structure and function.

Materials and Methods: In this study, a biocompatible gelatin type B-based hydrogel scaffold (10% w/v) was fabricated and functionalized with human costal cartilage powder and manganese oxide (MnO₂) nanoparticles at varying concentrations to enhance biological performance and better mimic the extracellular matrix microenvironment of the intervertebral disc. To evaluate the scaffold properties, Fourier-transform infrared spectroscopy (FTIR), pH stability, degradability, and hemocompatibility assays were conducted.

Results: FTIR analysis confirmed the presence of characteristic gelatin functional groups, cartilage-derived components, and surface interactions of MnO₂ nanoparticles. Degradability assessments demonstrated gradual and controlled scaffold decomposition, during which pH values remained within physiological limits, indicating the preservation of chemical homeostasis without the generation of harmful acidic or alkaline byproducts. Moreover, hemocompatibility tests revealed no cytotoxic effects and indicated favorable interactions between the scaffold and blood components.

Conclusion: The results show that the designed nanocomposite, with its desirable biocompatibility, controlled degradability, and chemical stability, is a suitable option for use in intervertebral disc reconstruction

Keywords: Tissue Engineering, Intervertebral Disc, Hydrogel, MnO₂ Nanoparticles,

Ps-142: Identification of Cell Cycle-Associated Therapeutic Targets in Hepatocellular Carcinoma (HCC)

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Objective: Hepatocellular carcinoma (HCC) is a prevalent and deadly form of liver cancer, with current systemic therapies often limited by off-target effects and significant side effects. Dysregulation of the cell cycle is a hallmark of cancer progression, including in HCC, making it a promising target for therapeutic intervention. This study aimed to identify potential therapeutic targets within the cell cycle pathway in HCC through integrative transcriptomic analysis, with the goal of repurposing existing FDA-approved drugs to improve treatment outcomes.

Materials and Methods: Transcriptomic data from HCC patients were retrieved from two public repositories: the microarray dataset GSE104310 from the Gene Expression Omnibus (GEO) and RNA-seq data from The Cancer Genome Atlas (TCGA). Differentially expressed genes (DEGs) were identified using the criteria of adjusted log₂ fold change (logFC) ≥ 1 and p-value < 0.05 . Functional enrichment and survival analyses were conducted to prioritize key cell cycle-related genes. Protein-protein interaction (PPI) networks and miRNA-gene interactions were constructed. Drug-gene network analysis was performed to identify FDA-approved drugs targeting the selected genes, followed by molecular docking studies to assess binding affinities between candidate drugs and target proteins.

Results: DEG analysis revealed significant overexpression of AURKA (Aurora kinase A) and CDC25C (Cell Division Cycle 25C), two critical regulators of the mitotic phase and G2/M transition in the cell cycle. High expression levels of these genes were associated with poor overall survival in HCC patients. PPI and miRNA network analyses highlighted their central roles in cell cycle regulation. Drug-gene network analysis identified several FDA-approved drugs with potential to target these proteins. Molecular docking suggested that some compounds, including cisplatin, show promising binding affinities to both AURKA and CDC25C, supporting their potential for repositioning in HCC treatment.

Conclusion: This integrative computational study highlights AURKA and CDC25C as promising therapeutic targets in hepatocellular carcinoma. The identification of FDA-approved drugs with strong binding affinities to these targets supports the feasibility of drug repositioning strategies. Targeting these cell cycle regulators may offer a more effective and less toxic approach for HCC treatment by inducing cell cycle arrest and inhibiting tumor progression.

Keywords: Hepatocellular Carcinoma, Machine Learning, cell cycle, Therapeutic Targeting,

Ps-143: Investigating The Effect Of Short And Long-Term Presence Of Lithium Chloride On The Electrophysiological Properties Of The Cultured Neural Network

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Objective: Lithium is widely used in the treatment of psychological disorders such as bipolar disorder and in nervous system trauma studies, such as spinal cord injuries. The mechanism of action of this drug and its effects on nerve cells are not fully understood; in vitro studies have identified that one of the most well-known effects of this drug is the inhibition of electrophysiological activities. One of the most important targets of this

drug is GSK-3 (glycogen synthase kinase 3), which it inhibits. One aspect that has been less studied is the effect of lithium on electrophysiological parameters at the neural network level. In this study, we created a two-dimensional neural network on a Multi Electrode Array plate and applied lithium long-term (7 days) to examine the effects of lithium on the electrophysiological parameters of the neural network.

Materials and Methods: In this study, we used the cortex of 16 to 18-day-old rat embryos, which were subjected to mechanical and enzymatic digestion, and the resulting cells were cultured on a Multi Electrode Array plate. After creating the neural network, a baseline recording was taken from all channels of the plate, and then lithium was applied at a concentration of 1.5 mM for seven days. Subsequently, recordings were taken again from the plates, and the resulting data were analyzed and compared.

Results: In the present study, while the two-dimensional neural network cultured from rat origin was successfully created, it was found that the application of lithium over seven days significantly increased the number of spikes (P value: 0.0088), the number of bursts (P value: 0.00076), and the mean amplitude of spikes (P value: 0.051).

Conclusion: The data show that the presence of lithium long-term shifts the balance of activity in the cultured neural network towards increased excitation and activity.

Keywords: Neural network, MEA, lithium, electrophysiology

Ps-144: Deciphering Umbilical Cord Blood Exosomes: Structural Insights for Advancing Regenerative Medicine

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Objective: Exosomes derived from umbilical cord blood have been identified as promising candidates for non-cellular therapeutic strategies in regenerative medicine. These extracellular vesicles (EVs) not only exhibit minimal immunogenic responses but also provide a versatile platform for drug delivery. This study aimed to characterize the structural properties of these exosomes to evaluate their potential for developing innovative regenerative therapies.

Materials and Methods: Exosomes were isolated through ultracentrifugation, including plasma centrifugation at 1500 rpm for 15 minutes at 4 °C, followed by 60,000 g for 90 minutes. The pellet was resuspended in sterile PBS, recentrifuged at 1000 g for 30 minutes, and stored at -80 °C. Structural analysis was performed via scanning electron microscopy (SEM), while flow cytometry identified molecular markers CD9, CD63, and CD81. Dynamic light scattering (DLS) measured the hydrodynamic diameter for precise size distribution.

Results: Flow cytometry confirmed the presence of CD9, CD63, and CD81, establishing the exosomal origin. SEM revealed spherical morphology with membrane definition, with dimensions ranging between 40 to 100 nm. DLS measured an average diameter of 53.5 nm, demonstrating uniformity and stability. These features emphasize their potential as non-cellular therapeutic agents.

Conclusion: The structural analysis of umbilical cord blood-

derived exosomes highlights their exceptional potential in regenerative medicine. With reduced immunogenicity, precise size distribution, and the ability to deliver bioactive molecules, these vesicles emerge as superior alternatives to stem cell-based therapies.

Keywords: Exosome, umbilical cord blood, Regenerative medicine

Ps-145: Investigation of the Effect of Zebrafish Embryonic Extract on Fibrosis-Associated Cells in Primary Biliary Cholangitis and Primary Sclerosing Cholangitis

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Objective: Primary Biliary Cholangitis (PBC) and Primary Sclerosing Cholangitis (PSC) are chronic liver diseases, often considered autoimmune conditions, in which the bile ducts of the liver become inflamed, leading to fibrosis and eventually narrowing or blockage. When this occurs, bile builds up in the liver, causing further damage and liver failure. The two conditions are very similar; Primary Biliary Cholangitis (PBC) is characterized by progressive destruction of the bile ducts within the liver while Primary Sclerosing Cholangitis (PSC) affects all of your bile ducts, including your intrahepatic bile ducts and extrahepatic bile ducts. These bile ducts are responsible for transporting bile, which aids in the digestion of fats. Currently, there isn't any specific clinical treatment method that can cure or halt the progression of either disease, so there remains a need for novel treatments targeting fibrosis in these conditions. Zebrafish embryonic extract (ZEE) has shown positive effects on breast cancer, intestinal cancer, liver carcinoma, melanoma, hair regeneration, sensorineural hearing, and mesenchymal stem cells. All these findings suggest that the effects of zebrafish embryonic extract might be important in tissue regeneration and repair; therefore, this research aims to investigate the potential impact of ZEE on cells involved in fibrosis associated with PBC and PSC.

Materials and Methods: This research will utilize in vitro cell culture models of hepatic fibrosis, including the hepatic stellate cell line (LX-2), to assess the effects of ZEE on fibrogenesis, cell proliferation, and activation rates. The changes in gene expression related to fibrosis in conditions of treated with ZEE will be evaluated.

Results: The MTT test results show that the viability of LX-2 cells increases when treated with ZEE. The changes in gene expression related to fibrosis under conditions treated with ZEE are being evaluated, and the molecular results will be reported soon.

Conclusion: Investigating the effect of Zebrafish embryonic extract on cells involved in fibrosis associated with primary biliary cholangitis and primary sclerosing cholangitis will provide valuable information related to the progression of fibrosis, potential treatments for these conditions, and ultimately, liver cell regeneration.

Keywords: Primary Biliary Cholangitis (PBC), Fibrosis, Zebrafish embryonic extract (ZEE), Hepatic stellate cells

Ps-146: Gold Nanoparticles Functionalized with BSA for Photothermal Therapy of MDA-MB231 Breast Cancer Cell Line

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Objective: Cancer is one of the most complex diseases which still has no definitive treatments while combination radiotherapy of surgery and chemotherapy are applied. Considering that metal nanoparticles, especially gold, have an advantage of high light-to-heat conversion efficiency, in the present study, gold nanospheres (GN) were prepared and coated bovine serum albumin (BSA) protein to be used on MBA-MB231 cells when treated with laser

Materials and Methods: GN were synthesized using Turkevich method and coated with BSA then characterized using UV-vis spectroscopy, dynamic light scattering (DLS), zeta potential measurement, and FTIR-ATR analysis. Using 400 and 800 µg/ml of GN, the MDA-MB231 cancerous cells were exposed to laser for 5 minutes and incubated for 24 hours. Subsequently, cell viability, nucleus and cytoplasm morphology, and DNA damage were investigated. Furthermore, oxidative stress induced by photothermal therapy based on malondialdehyde production, changes in total antioxidant capacity and the activity of catalase and superoxide dismutase were estimated. Then the mechanism of cell death was examined using DNA ladder and flow cytometry analysis.

Results: The synthesized nanoparticles were spherical and 77.35±9.56 nm in size. Their IC₅₀ was determined to be approximately 800 µg/ml and statistical analysis of the data showed that laser irradiation of the BSA coated gold nanoparticles (BSA-BN) significantly induced oxidative stress in MDA-MB231 cells compared to the group treated with nanoparticles without laser irradiation. Additionally, the morphology of the treated cells revealed chromatin condensation, nuclear size reduction, and cytoplasmic shrinkage, where agarose gel electrophoresis showed that treatment of MDA-MB231 cells with BSA-GN and laser irradiation led to DNA fragmentation, forming a ladder pattern. Flow cytometry confirmed that the treatment caused apoptosis in the cells.

Conclusion: Although in vivo studies are essential, the results showed coating GN with BSA effectively induce oxidative stress and apoptosis in MDA-MB-231 cells after laser irradiation.

Keywords: Photothermal therapy, Bovine serum albumin, Gold nanoparticles, Apoptosis, Cancer cell

Ps-147: Establishment of ovarian patient-derived tumor organoid for drug screening

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Objective: Ovarian cancer (OC) is one of the most challenging gynecological cancers with a poor prognosis due to late-stage diagnosis and high recurrence rates. Therefore, there is a critical need for preclinical models that can replicate patient-specific histopathological and molecular heterogeneity to support personalized treatment approaches. To address this gap, we established ovarian cancer organoids as an advanced organ culture model to predict drug responses and demonstrate inter-patient variability.

Materials and Methods: In this study, we established patient-derived tumor organoid cultures from high-grade serous carcinoma (HGSC) ovarian cancer. The tumor organoids were characterized based on culture efficacy, and gene and protein expression through RT-PCR and confocal microscopy. Patient-derived organoids (PDOs) preserved the histological and molecular heterogeneity of the parental tumors. A drug screening pipeline was implemented using PDOs, testing standard-of-care (cisplatin) and FDA-approved compounds (JQ1) for other cancer types.

Results: The ovarian tumor organoids demonstrated high expression of specific ovarian cancer markers such as ERB, Era, CD44, CK8, and Ki67. Other ovarian-specific markers showed varying levels of expression. Quantification of immunofluorescence imaging revealed a 3D structure of organoids with high expression of Ki67, and E-cadherin. Drug screening showed the combination of cisplatin and JQ1 significantly decreased the viability of PDO.

Conclusion: Our study suggests that monitoring ovarian tumor drug responses using the ovarian organoid model can serve as a reliable platform to determine and optimize patient-specific treatment strategies, providing valuable insights for personalized medicine.

Keywords: Tumor organoid, Ovarian cancer, Drug screening, Personalized medicine

Ps-148: Downregulation Of Itih4-As1 in Patients with Bipolar Disorder

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Objective: Bipolar disorder is a type of chronic disorder recognized by sudden and extreme changes in a person's mood and temperament. The neurobiological mechanisms of bipolar disorder are not fully understood and are evolving. The JAK-STAT signaling pathway plays a nuanced role in early neuronal development, primarily through regulating neural stem cell (NSC) proliferation and maintenance rather than directly driving neurogenesis. Long-None coding RNAs are a new type of None-coding RNAs that play different roles in cell. The long non-coding RNA ITIH4-AS1 plays a significant role in activating the JAK-STAT3 signaling pathway and therefore can play

a key role in development of neuron progenitor cells. In this study we investigate the association of ITIH4 and bipolar disorder by monitoring its expression levels.

Materials and Methods: We performed Real-time PCR for 50 patients of bipolar disorder as case and compared them with 50 healthy individuals as control.

Results: Our results showed that ITIH4 was expressed significantly in bipolar patients compared to healthy controls ($P = 0.0028$).

Conclusion: In conclusion, results highlight that the dysregulation of ITIH4 may be associated with an increased risk of BD. Further study is recommended to better investigate the functions of this lncRNA in early stages of neural development.

Keywords: Bipolar disorder, Real-time PCR, Long-None-coding RNA, ITIH4, Stem cells

Ps-149: GMP-Compliant Protocol for Differentiation of Human Embryonic Stem Cells into Definitive Endoderm

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Objective: Human embryonic stem cells (hESCs) are promising candidates for cell-based therapies in different diseases due to their ability to differentiate into different lineages. Various emerging endodermal lineage cell-based therapies, including those for Type 1 diabetes, require the production of GMP-grade hESC-derived definitive endoderm (hESC-DE) cells. This study aims to generate hESC-DE using a GMP-compliant protocol for use in subsequent differentiation steps towards pancreatic cells or potentially any other endodermal derivatives.

Materials and Methods: We established an optimized framework for evaluating the starting material, including the selection and qualification of hESC lines, as well as validating the stepwise differentiation protocol, including the differentiation procedure and ancillary materials. The identity of the resulting DE cells was confirmed using quantitative real-time PCR (qRT-PCR), immunostaining, and flow cytometry, targeting key markers such as SOX17, FOXA2, CD184, and CD117. These analyses contributed to the development of a certificate of analysis (CoA) for the hESC-DE product

Results: We optimized the differentiation protocol by adding adjusted concentrations of ITS-X and FBS as supplements to the base medium and eliminating basic fibroblast growth factor and ascorbic acid from our previously published hESC-DE differentiation protocol. Our final product (hESC-DE) was evaluated and confirmed by the expression of FOXA2, SOX17, CD184, and CD117 markers measuring by qRT-PCR, Immunostaining and flow cytometry analysis.

Conclusion: Our results demonstrate that hESC-DE cells can

be generated with suitable efficiency and defined specifications under a GMP-compliant protocol. These cells represent a viable primary source for the production of endodermally derived cell types in cell therapy applications.

Keywords: GMP-compliant, Definitive endoderm, Ancillary material, Differentiation, Type 1 Diabetes, Cell therapy

Ps-150: Development of an siRNA Design Algorithm to Improve Gene Silencing Efficiency Considering mRNA Secondary Structure and Immune Response

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Objective: RNA interference (RNAi) has emerged as a powerful tool for gene silencing, with small interfering RNAs (siRNAs) playing a central role. In siRNA design, silencing efficiency and immune response are two crucial factors that significantly influence their applicability in research and therapeutics. Optimizing these parameters is essential to enhance siRNA efficacy while minimizing off-target effects.

Materials and Methods: Conventional siRNA design workflows typically include three stages: identifying 23-nucleotide functional candidates based on empirical rules, removing sequences with undesirable seed melting temperatures to reduce off-target effects, and genome-wide homology screening to avoid random sequence similarity. In this study, we propose an extended four-step computational algorithm. The first three steps align with standard methodologies, while the fourth step incorporates secondary structure information of the target mRNA.

Results: By predicting the mRNA's folding pattern, the algorithm prioritizes siRNA candidates that bind to regions with higher nucleotide unpairing (greater local openness), which are more likely to be accessible and thus efficient in gene silencing. Moreover, to address potential immunogenic effects in vivo applications, the algorithm includes a screening step for immunostimulatory motifs previously identified to activate innate immune responses.

Conclusion: This dual consideration of mRNA structural accessibility and immunogenicity risk represents a comprehensive and rational strategy for selecting siRNA sequences. The algorithm aims to provide a refined tool that enhances both the silencing efficiency and safety of siRNAs for future experimental or clinical use.

Keywords: siRNA design, mRNA secondary structure, RNA immunogenicity, RNA fold, small RNA

Ps-151: Efficient Silencing of Oct4 and Nanog in Mouse ESCs Using Optimized siRNAs with Minimal Immune Activation

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Objective: The Oct4 and Nanog genes are among the most critical regulators in maintaining the pluripotency of stem cells. One of the approaches for inducing differentiation is the suppression of these genes using small interfering RNAs (siRNAs). Conventional siRNA design methods typically aim for weak seed-region binding and minimal sequence complementarity with off-target genes.

Materials and Methods: In this study, candidate siRNAs were initially designed using standard approaches, then prioritized based on mRNA secondary structure and target site accessibility. Additionally, candidates containing immunostimulatory motifs were identified. To validate the design strategy, four siRNAs were selected and synthesized, each representing a specific feature: targeting a fully open region, a fully closed region, containing immunostimulatory motifs, or lacking such motifs.

Results: We found that all siRNAs significantly downregulated the respective target transcripts in embryonic stem cells (ESCs), as evidenced by qRT-PCR results. Importantly, siRNAs targeting open regions showed significantly greater suppression than the ones targeting the closed regions, judging from qRT-PCR and flow cytometry assays. This observation was also associated with a marked decrease in cell viability and pluripotency, based on the alkaline phosphatase staining and MTS viability results. Finally, analysis of inflammatory markers revealed that siRNAs containing immunostimulatory motifs elicited significantly stronger immune responses than those without such motifs.

Conclusion: Due to their higher silencing efficiency and reduced immunogenicity, the designed siRNAs hold potential for inducing exit from pluripotency in stem cell- and developmental studies.

Keywords: RNAi, gene silencing, Pou5f1, self-renewal, differentiation

Ps-152: Downregulation of CBR3-AS1 in Patients with Bipolar Disorder

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Objective: Bipolar disorder (BD) is a severe condition that is often accompanied by many symptoms that can include periods of mania and depression. Despite recent advances in the neurobiology of Bipolar disorder, the exact cause remains unclear and even unknown. There is evidence of an association between bipolar disorder and early development of neuron cells and its biological pathways. Scientists have reported that NOTCH signaling pathway is an evolutionarily conserved mechanism that regulates cell fate decisions during development and maintains tissue homeostasis. In the early stages of neural development, NOTCH signaling plays a critical role in establishing neural domains and controlling the fate of neural progenitor cells (Balancing Neuronal and Non-Neuronal Fates). CBR3-AS1 plays a significant role in this pathway. In recent studies on the CBR3-AS1 gene, scientists observed that this gene is transcribed to a new group of non-coding RNAs called LncRNAs (Long None-Coding RNAs) that play a wide range of roles, especially in developing and maintaining normal functions of neuron cells, especially brain cells.

Materials and Methods: Here we aimed to evaluate the ex-

pression of CBR3-AS1 in 50 patients with bipolar disorder and 50 healthy individuals as control by performing real-time PCR.

Results: Our data revealed significantly lower expression levels of CBR3-AS1 lncRNA in patients with Bipolar Disorder compared with control individuals ($P=0.0012$).

Conclusion: In conclusion, the obtained results demonstrate that CBR3-AS1 lncRNA may have a pleiotropic role in BD pathogenesis. We assume downregulation of this lncRNA in early stages of neural development can lead to developing psychological disorders such as Bipolar Disorder, which requires further study.

Keywords: Bipolar Disorder, Long Non-coding RNAs, CBR3-AS1, Neural development, Notch signaling pathway

Ps-153: Applications of Artificial Intelligence in Stem Cell Research: A Systematic Review of Trends, Tools, and Translational Potential

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Objective: Artificial intelligence increasingly transforms stem cell research by enabling efficient analysis of complex datasets while reducing study costs and time. Despite these advances, practical applications and clinical translation remain fragmented, prompting an examination of image analysis, differentiation modeling, and predictive biology tools.

Materials and Methods: A thorough search was conducted in PubMed for studies published between 2015 and 2024 using terms related to AI and stem cells. Inclusion criteria targeted original research articles applying AI methods directly to stem cell-related questions, with study quality assessed following PRISMA guidelines.

Results: This systematic review analyzed 30 studies to explore the application of artificial intelligence (AI) in stem cell data analysis. Eighteen distinct AI algorithms were identified, including deep learning, traditional machine learning, clustering, and dimensionality reduction methods. The most frequently used techniques were convolutional neural networks (CNNs), random forests, support vector machines (SVMs), and UMAP. AI models were applied to diverse data types such as microscopy images, bulk and single-cell RNA sequencing, epigenetic profiles like ATAC-seq and DNA methylation, and metabolomics. CNNs were primarily used for image-based classification of stem cell states, while single-cell RNA-seq data benefited from clustering and trajectory inference methods like UMAP and Louvain algorithms. Key functional applications included predicting cell differentiation pathways, identifying stem cell subpopulations, selecting gene markers, and generating synthetic data. Notably, 10 studies focused on inferring differentiation trajectories, and at least 8 emphasized single-cell data analysis. This review underscores the expanding role of AI in stem cell research, showcasing its ability to manage complex biological data and reveal hidden patterns in cellular behavior. Nonetheless, challenges remain in standardizing datasets and benchmarking AI models, which are critical areas for future investigation.

Conclusion: In conclusion, AI is a transformative tool in stem cell research; however, to fully realize its translational impact, further standardization and clinical validation of AI methods

are necessary.

Keywords: Artificial Intelligence, Stem Cell, CNNs

Ps-154: An *In Vitro* Study of The Nanoplastics-Induced Cytotoxicity on Endothelial Cells

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Objective: Nanoplastics (NPs) are emerging as one of the potential risk factors related to the development of cardiovascular diseases (CVDs) among the broad range of possible health effects. Several studies have provided evidence supporting the hypothesis that NPs activate a variety of pathophysiological pathways in cells involved in CVDs pathophysiology. In light of the importance of NPs in this field, pioneering experiments are crucial for obtaining a more comprehensive understanding of the underlying mechanisms. In this study, we aimed to address this need by focusing our research accordingly.

Materials and Methods: Human umbilical vein endothelial cells (HUVECs) were initially seeded in a 96-well plate at 2×10^4 cells/well for 24h in DMEM/F12 supplemented with 10% fetal bovine serum and incubated at 37 °C and 5% CO₂. HUVECs were exposed to different doses of polystyrene NPs (5-400 µg) for 48 h. To determine the survival rate of the cells, the Methyl Thiazolyl Blue Tetrazolium Bromide (MTT) assay was performed at 570 nm using a microplate reader.

Results: The findings showed that polystyrene NPs at a dose of 5µg increased cell viability when compared with higher doses. Contrary to the lower doses, intermediate doses demonstrated moderate loss of viability, while higher doses (e.g., 200 and 400 µg) were cytotoxic.

Conclusion: As shown by the dose-dependent trend of polystyrene NPs, lower concentrations appear to be less harmful and even slightly stimulating, while higher concentrations result in progressive declines in HUVEC survival. Nonetheless, these results indicate that further research is required to define safe exposure levels.

Keywords: Cardiovascular diseases, Endothelial cells, Nanoplastics, Cell viability

Ps-155: In Vitro Assessment of Genotoxicity in CAR T-Cells Generated with Retroviral Vectors

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Objective: Chimeric Antigen Receptor (CAR) T-cell therapy has shown significant efficacy in the treatment of hematological malignancies, particularly those associated with B lymphocytes. The CAR construct, usually introduced into T-cells via viral vectors for stable and efficient gene expression, raises

concerns regarding insertional mutagenesis and genotoxicity. Unintended integration events and inappropriate multiplicity of infection (MOI) may lead to genomic instability and increase the risk of malignant transformation. In November 2023, the U.S. Food and Drug Administration (FDA) reported rare but serious cases of T-cell lymphoma following CAR T-cell therapy. Although these events are rare, they underline the critical importance of sensitive and standardized genotoxicity testing.

Materials and Methods: Peripheral blood mononuclear cells (PBMCs) were isolated and transduced using a retroviral vector encoding the anti-CD19 CAR construct. The sensitivity of the genotoxicity detection method, optimal time-frame for evaluation, and safe transgenic copy number threshold were assessed in three phases of the experiment. Cell proliferation and viability were assessed by flow cytometry-based assays, including Ki67 staining, CFSE dilution and cell cycle analysis. Copy number was further evaluated by quantitative PCR (Q-PCR).

Results: Results showed that clonal expansion could be detected with a sensitivity of approximately 1%, a reliable threshold for early detection of the emergence of unintended cell lines. This was compared with CD3 labeling used to identify target T cells. Day 6-7 after removal of growth factor was identified as the most informative point for detection of abnormal cell expansion.

Conclusion: Our findings demonstrate an in vitro approach to product safety assessment that promotes regulatory compliance and contributes to mitigating risks. While the overall risk of transformation is low compared to other therapies, continued vigilance and rigorous testing is essential to ensure that CAR T-cell therapy continues to be safe.

Keywords: CAR T-cell, Retroviral vector, Genotoxicity, Copy number, multiplicity of infection (MOI)

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