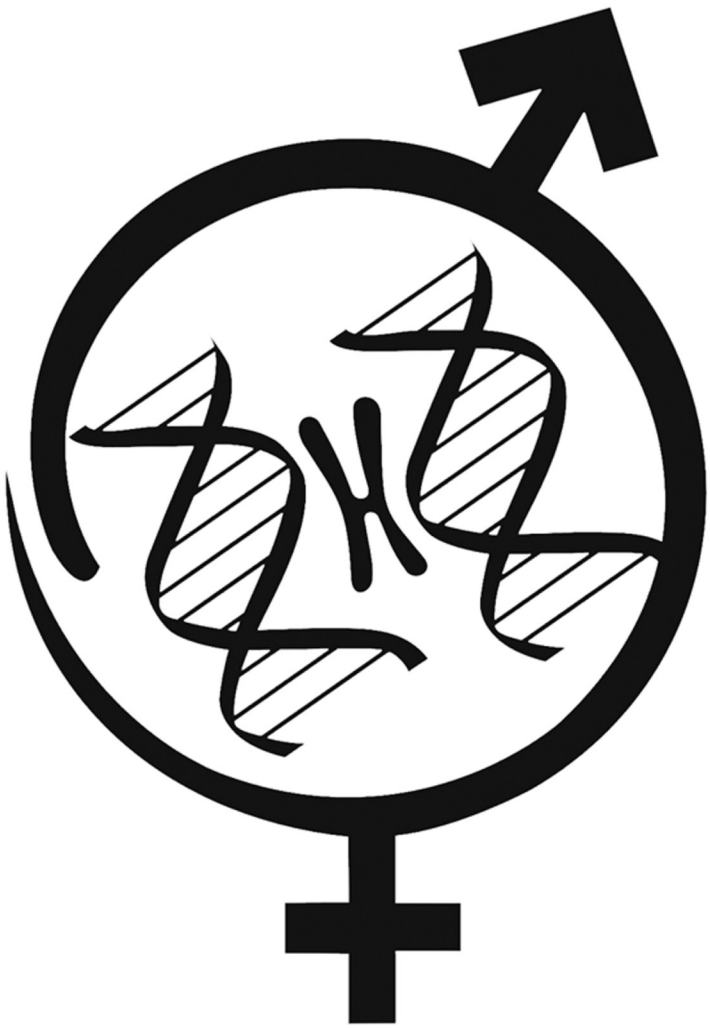
Abstracts of

Royan International Hybrid Twin Congress

20th Congress on Stem Cell Biology and Technology
28-30 August 2024



Royan Institute

Cell Science Research Center

Tehran, Islamic Republic of Iran

Abstracts of the 20th Congress on Stem Cell Biology and Technology (2024)

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Congress Chairperson

Leila Taghiyar

On behalf of the organizing committee, it is my great pleasure to welcome you to the "20th International hybrid Congress on Stem Cell Biology and Technology (ICSCBT), 28-30 August 2024, Tehran, Iran".

The ICSCBT is an international annual gathering in stem cell research and regenerative medicine covering both basic and translational contents in Iran. So, the brightest thoughts in stem cell research from worldwide, and disciplines will discuss impediments, and innovation, and share recent cutting-edge research in the field of stem cells.

Royan Institute was established in 1991 by the late Dr. Kazemi Ashtiani. As a pioneer Institute, the Royan Institute for Stem Cell Biology and Technology (RI-SCBT) embraced stem cell basic and translational studies, developmental biology, and regenerative medicine.

We kindly invite you to join us and invited scientists from around the world at ICSCBT 2024 for a 3-day program featuring the year's most significant new developments in the field, in the historical/ multicultural city of Tehran.

Kind regards
Leila Taghiyar, PhD
Chairperson of 20th Royan International Virtual Congress on Stem Cell Biology & Technology

Invited Speakers

Is-1: Empowering Parents for Early Childhood Development: A Journey with Kidora

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Kidora is a pioneering startup committed to empowering parents and enhancing early childhood development through scientific solutions. The first five years of a child's life are crucial for brain development, and Kidora aims to bridge the gap between busy parents and their children's need for enriched experiences during this formative period. By collaborating with experts and offering expert-backed programs and resources, Kidora provides parents with the knowledge, tools, and confidence to nurture their child's mental development effectively.

Is-2: Immune Cell Therapy: Side Effects, Risks and Limitations in Cancer

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Immune cell therapies, particularly Chimeric Antigen Receptor T-cell (CAR-T) therapies, have revolutionized the treatment landscape for various hematological malignancies and hold promise for solid tumors. Despite their remarkable efficacy, these therapies are accompanied by significant side effects, risks, and limitations that necessitate careful consideration and management. CAR-T cell therapy has demonstrated substantial success in treating certain cancers, but it also poses risks of severe toxicities. Common adverse effects include cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). CRS, characterized by fever, hypotension, and multi-organ dysfunction, occurs due to massive cytokine release following CAR-T cell activation and proliferation. ICANS, presenting as encephalopathy, seizures, and cerebral edema, represents another major toxicity that can significantly impact patient outcomes. Additionally, CAR-T cell therapy is associated with unique cardiac toxicities, as detailed in recent studies. Adverse cardiac effects, such as arrhythmias, cardiomyopathy, and heart failure, necessitate vigilant cardiac monitoring and management strategies. The long-term outcomes of CAR-T cell therapy also reveal persistent cytopenias, hypogammaglobulinemia, and secondary malignancies, highlighting the need for ongoing surveillance and supportive care. The review further explores the limitations of CAR-T cell therapy, including antigen escape, tumor heterogeneity, and limited efficacy in solid tumors. The identification of target antigens and the development of strategies to overcome these challenges remain critical for expanding the applicability of CAR-T cell therapies. Emerging data from clinical studies underscore the importance of balancing efficacy with toxicity management. Strategies such as optimized CAR design, early intervention for toxicities, and combination therapies are being investigated to enhance the safety and effectiveness of CAR-T cell treatments.

Is-3: Liver Gene Therapy Platform for Therapeutic Induction of Immunological Tolerance in Type 1 Diabetes

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The liver gene therapy platform for Type 1 Diabetes (T1D) leverages the liver's inherent tolerogenic properties by targeting hepatocytes with lentiviral vectors (LVs) to induce antigen-specific tolerance. By delivering genes encoding the insulin B chain 9-23 (InsB9-23), an immunodominant T cell epitope, to hepatocytes, the therapy promotes the generation of both effector T cells and FoxP3(+) regulatory T cells (Tregs), which prevent islet immune cell infiltration and protect against T1D. Combining this gene therapy with a suboptimal dose of anti-CD3 monoclonal antibody (mAb) has shown efficacy in reversing T1D in nonobese diabetic (NOD) mice. The antigen-specific nature of the protection is confirmed by the ability of splenocytes from treated mice to halt diabetes development in other mice. Integrase-defective LVs (IDLVs) offer a safer alternative by mitigating concerns about insertional mutagenesis while still effectively protecting against T1D. This approach aims for long-term immune tolerance without continuous therapy, presenting a promising strategy for managing autoimmune diseases. Future directions include optimizing vector design and delivery methods for broader applications in other autoimmune diseases, allergies, and organ transplantation, with ongoing research focused on facilitating the transition from preclinical models to human trials.

Is-4: Biomimetic Smart Theranostic Platforms

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Tailored drug delivery system-based nanocarriers have been intensively studied and developed for use in clinical oncology. Currently, the fundamental mechanism of tumor-specific nanocarrier uptake is achieved through increased permeability and retention effects. However, the immune system recognizes and eliminates the majority of nanoparticles, thereby limiting their therapeutic use. Therefore, it is crucial to develop safer and more effective methods. One of the most promising platforms in this context is biomimetic nanoparticles decorated with bioactive membranes. These nanoparticles versatility as well as the adaptability of NPs along with the intricacy and utility of cell membranes could lead to significant changes to the tumor microenvironment. In our laboratory, we actively worked on biomimetic drug delivery systems. For instance, we fabricated a platform by combining a cationic lipid, 1,2-Dioleoyl-3-trimethylammonium-propane (DOTAP) with mesenchymal stem cell membrane (MSCM) to produce a positively charged

hybrid vesicle. The prepared hybrid vesicle was used to condense BIRC5 CRISPR/Cas9 plasmid for survivin (*BIRC5*) gene editing against melanoma. In another study, MSCs-derived exosomes were used as carrier for oxygen and doxorubicin delivery to tumor site. As an approach, oxygen delivery could provide tumor oxygenation, enabling ultrasound imaging. In this regard, the surface of the exosomes was also coated with a Sgc8-c aptamer against protein tyrosine kinase (PTK-7). Furthermore, by different cells membrane coating strategies, multimodal inorganic nanoparticles were prepared for cancer treatment and imaging. Based on our investigation, the application of biomimetic vehicles provides a potentially safe strategy for cancer therapy and has great potential for clinical translation.
Keywords: Biomimetic, Exosome, Mesenchymal Stem Cell Membrane, Nanobubble

Is-5: Glioblastoma Gene Therapy: Using Cocktail Constructs

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Glioblastoma multiforme (GBM) is a highly aggressive and deadly brain cancer that remains incurable with standard treatments. MicroRNAs (miRNAs) hold significant promise for gene therapy due to their ability to regulate multiple target genes simultaneously. Our research identified several miRNAs, which inhibit the cell cycle and induce apoptosis in glioblastoma cells. These miRNAs have predicted target genes across various signaling pathways, analyzed through bioinformatics tools, and validated by experimental methods such as luciferase assays, Real-Time PCR, and western blotting. Treating brain tumors, particularly GBM, remains challenging due to the lack of efficient drug delivery systems. However, the combined use of microRNA and the suicide gene (SG), along with the prodrug, induced cytotoxicity in glioma cells in vitro. Overexpression of SG/miR in the presence of prodrug significantly enhanced apoptosis and caused cell cycle arrest in these cells. Our findings demonstrate the effectiveness of drug delivery using engineered apoptosis-inducing exosomes and highlight the improved apoptosis achieved through this combination approach. In animal models, apoptosis induction and tumor growth inhibition were significantly greater in those carrying SG/miR compared to the control group.
Keywords: Glioblastoma Multiforme, microRNAs, Gene Therapy, Cytosine Deaminase

Is-6: Stem Cells, Nanotechnology and Regenerative Medicine

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Integration of new developing sciences like biomedicine with other engineering and biomaterial sciences promoted the development of nanotechnology and regenerative medicine with potential to revolutionise modern medicine leading to non-invasive and more efficient treatments.
Nanotechnology plays a crucial role in enhancing the effectiveness of stem cell therapies. Nanomaterials can be engineered to create scaffolds that mimic the natural extracellular matrix, providing a supportive environment for stem cells to grow and differentiate. These scaffolds can be designed to release growth factors and other signalling molecules in a controlled manner, promoting the development of specific cell types needed for tissue regeneration.
Nanoparticles can also be used to deliver drugs directly to stem cells or the site of injury, improving the efficiency of regenerative treatments. For example, nanoparticles can be loaded with drugs that promote stem cell survival and differentiation, ensuring that the stem cells function optimally once they are transplanted into the body.
Anyhow nanotechnology also enhances the ability to image and track stem cells in the body. Nanoparticles can be designed to be visible under various imaging modalities, such as MRI or fluorescence microscopy. This allows researchers and clinicians to monitor the distribution, migration, and integration of stem cells in real-time, providing valuable insights into the effectiveness of regenerative therapies.
In regenerative medicine, tissue engineering involves creating bioengineered tissues and organs that can replace damaged ones. Nanotechnology contributes to this field by providing materials that can be used to construct these tissues. For instance, nanofibers can be used to create scaffolds that support the growth of stem cells into functional tissues, such as skin, cartilage, or even more complex organs.
As conclusion, the integration of stem cells, nanotechnology, and regenerative medicine is a rapidly evolving field with immense potential. Future research may focus on developing more sophisticated nanomaterials that can precisely control stem cell behaviour, creating more effective and personalized regenerative therapies. Additionally, advances in nanotechnology may lead to new ways to deliver stem cells and therapeutic agents to specific tissues, further improving the outcomes of regenerative treatments. These interconnected fields are paving the way for innovative medical treatments that could revolutionize healthcare and improve the quality of life for many patients.

Is-7: Bioceramics-Based 3D Printed Scaffold for Bone Tissue Engineering

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Tissue engineering has a special place in the field of bone damage reconstruction. Meanwhile, scaffolds are one of the most important parts of a bone tissue engineering system. Although there are several conventional methods for the fabrication of bone scaffolds; recently, 3D printing techniques have been dramatically considered for this purpose due to their capabilities such as the creation of a controllable complex internal and external structure at the micro-scale. Among the 3D printing methods, the robocasting technique as an extrusion-based method is highly regarded especially for designing ceramic-based scaffolds. In this research, a three-dimensional 45S5 bioactive glass (BG) doped by zinc (3, 9, and 15%) and cobalt ions (1, 3, and 5%) /β-tricalcium phosphate (TCP) composite (50/50 wt. %) scaffold was prepared by the robocasting method. For this aim, BG and TCP were synthesized and characterized. The scaffolds were prepared by extruding the ink composed of a proper amount of BG, TCP, and required additives, then analyzed in

terms of physicochemical and biological properties. The fabricated 3D-printed scaffolds showed a hierarchical structure with regular and uniform porosities with a higher range of mechanical properties compared with the scaffolds with the same composition prepared with the foam casting method. In addition, the scaffolds doped with Zinc and cobalt showed improved mechanical strength, bioactivity, cell viability, and cell attachment compared to the undoped scaffolds. It also showed the important role of zinc and cobalt ions in improving osteogenic properties and, as a result, the expression of osteogenic genes and proteins. This study proved that the prepared scaffolds hopefully may be used for bone tissue engineering even in load-bearing defects.

Is-8: Personalized Medicine: from Molecular Phenotyping to Regenerative Medicine

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Personalized medicine has emerged as a promising approach in the treatment of a wide range of human diseases, aiming to tailor medical decisions to the individual characteristics of each patient. Initially, the focus lies on molecular phenotyping techniques which have revolutionized diagnosis by unraveling the molecular intricacies underlying diseases. These techniques, mainly next-generation sequencing (NGS), enable the identification of specific molecular signatures and biomarkers, paving the way for targeted therapies tailored to individual patients. It is worth noting that the integration of bioinformatics and artificial intelligence will cast a flash of light on the complex molecular datasets to predict treatment responses with unprecedented accuracy.
Moreover, the advent of regenerative medicines has opened new horizons in personalized medicine, encompassing innovative strategies such as cell-based therapies, gene therapies, tissue engineering, and organoids. These approaches hold immense potential for generating patient-specific models to elucidate disease mechanisms, screen drug candidates, and ultimately, engineer personalized therapies with enhanced efficacy and safety profiles. In summary, this presentation underscores the transformative impact of personalized medicine in human diseases, highlighting its journey from molecular phenotyping to the frontier of regenerative medicines, and emphasizing its profound implications for improving patient outcomes in the era of precision medicine.

Is-9: Requirements of stem cell-mediated skeletal muscle regeneration

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Contraction of skeletal muscles is mediated by syncytial myofibers, containing a highly specialized contractile apparatus maintained by large numbers of post-mitotic myonuclei. Adult skeletal muscle fibres are terminally differentiated and cannot be replenished without the help of muscle stem cells (MuSC), closely attached to myofibers and situated below the basal lamina. We have studied the transcriptional networks necessary to generate and maintain muscle cells from uncommitted mesodermal progenitor cells during embryonic development. Furthermore, we investigated the requirements of stem cell-mediated skeletal muscle regeneration. We discovered that the H4K20 methyl transferase Kmt5b is essential to maintain a high level of heterochromatin in muscle stem cells (MuSCs), whose depletion promotes exit of MuSCs from quiescence. We also found that loss of heterochromatin in Kmt5b-deficient MuSCs leads to aberrant transcription during S-phase, facilitating transcription replication collisions and genome instability. We concluded that transcriptional regulation of chromatin modifiers controlling heterochromatin formation is decisive to keep MuSCs in a quiescent state and to maintain nuclear architecture. Thus, we searched for transcription factors or transcriptional co-factors that may play a role in the regulation of chromatin modifiers in MusCs, Surprisingly, we identified TAF4A, primarily known as a subunit of the general transcription factor TFIID, as critical for genome stability and quiescence of MuSC. TAF4A is necessary for expression of Kansl2, which together with MOV is part of the non-specific lethal (NLS) complex, acetylating nuclear lamin A/C. Impaired acetylation of lamin A/C decreases stiffness of MuSC nuclei and disrupts the nuclear architecture. The subsequent loss of heterochromatin and MuSC activation, in combination with pronounced genomic instability, activates MuSCs and impairs MuSC proliferation. Furthermore, we found that Piezo1, a mechanosensitive ion channel, keeps MuSCs in a quiescent state and prevents senescence. Inactivation of Piezo1 results in compensatory up- regulation of T-type voltage-gated Ca2+ channels, leading to increased Ca 2+ influx, which strongly induces NOX4 expression via cPKC. Elevated NOX4 expression increases ROS levels and DNA damage, causing P53-dependent cellular senescence and cell death of MuSCs. Pharmacological inhibition of P53 in Piezo1-deficient mice abrogates increased senescence of MuSC and normalizes muscle regeneration. Reduced mechanosignaling due to decreased physical activity during aging may contribute to the increase of senescent cells and the decline of MuSC numbers in geriatric mice and humans.

Is-10: Reprograming the heart for regeneration

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Ischemic cardiomyopathy is the single largest cause of death in countries of all income groups. Remarkable progress in the treatment of acute myocardial infarctions has improved the outcome but the loss of myocardial tissue eventually leads to heart failure, showing an alarming increase in recent years. Unfortunately, the heart is a notorious non-regenerative organ, lacking dedicated stem cells, which complicates regenerative therapies. Terminally differentiated adult cardiac muscle cells only show a very low renewal rate in mice and man, insufficient for efficient organ regeneration after massive insults. In contrast, cardiomyocytes are still dividing during fetal and neonatal stages, permitting heart regeneration. This capacity that is lost shortly after birth concomitant with cardiomyocytes maturation, including a profound switch of the cellular metabolism. Mammalian cardiomyocytes become filled with sarcomeres and mitochondria, essentially creating pseudo-crystalline structures that

prevent cytokinesis. Reversal of this process, essentially a re-winding of the developmental program, may re-enable division of cardiomyocytes for replacement of lost contractile tissue and successful organ regeneration.
We have pursued several different strategies to rewind the development program for stimulation of heart regeneration. We found that microRNAs of the miR-1/133a family are instrumental for suppression of two crucial regulatory circuits controlling postnatal cardiomyocyte proliferation and dedifferentiation, the FGFR and OSMR pathways. Concomitant inactivation of both miR gene clusters in postnatal cardiomyocytes activates expression of cell cycle regulatory genes and cell-cycle re-entry of adult cardiomyocytes. We also found that heart-specific expression of OSKM (Oct4(O), Sox2(S), Klf4(K) and c-Myc(M)) converts cardiomyocytes to a fetal-like state, conferring regenerative capacity to adult hearts. Short-term OSKM expression before and during myocardial infarction ameliorates myocardial damage and improves cardiac function, demonstrating that temporally controlled dedifferentiation and reprogramming of cardiomyocytes facilitates heart regeneration. Inactivation of the miR-1/133a gene family as well as short-term cardiomyocyte-specific expression of OSKM reprograms heart metabolism from oxidative phosphorylation to more anaerobic energy-producing pathways. We therefore asked whether abrogation of fatty acid oxidation (FAO) in cardiomyocytes is sufficient to induce cardiomyocyte de-differentiation, proliferation and eventually heart regeneration. We discovered that inhibition of FAO after ischemic injury nearly full restores cardiac function, which is caused by accumulation of α-ketoglutarate, leading to activation of the α-ketoglutarate-dependent lysine demethylase KDM5. Activated KDM5 demethylates broad H3K4me3 domains in genes that drive cardiomyocyte maturation, lowering their transcription levels and shifting cardiomyocytes into a less mature state, promoting proliferation. Our studies provide fascinating perspectives for future clinical applications.

Is-11: Computational and Experimental Cardiac Flow Assessment: *In vitro*, *In vivo*, Clinical

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Cardiovascular diseases often manifest under disturbed hemodynamics conditions. Hence it is important to assess disturbed hemodynamics under clinical settings as well as for *in vitro* and *in vivo* experiments as part of cardiovascular research. In our studies, we focus on mechanobiology of severe cardiac diseases such as aortic aneursyms, aortic valve disease and cardiomyopathy, where we combine several bioengineering approaches including computational fluid dynamics modeling, and machine learning, to investigate progression of the conditions as well as for advancement of therapies. For clinical investigation, we investigate rupture risk assessment of aortic aneursysms, and predictive modeling of transcatheter aortic valve replacements. For *in vitro* studied, we develop micro pump systems enabling dynamic culture of cardiac cells within microfluidics system. For *in vivo* experiments, our main animal model is Zebrafish embryo due to its transparent nature enabling visualization and assessment of blood flow. In this lecture, I will be presenting our latest findings on cardiovascular mechanobiology.

Is-10: Nanostructures as Novel Drug Delivery Systems: Fundamental Issues and Market Perspectives

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Rassoul Dinarvand, received his Pharm.D. from University of Tehran in 1988. He then successfully completed his Ph.D. in the field of Controlled Drug Delivery Systems at the University of Manchester in 1993. He then joined Faculty of Pharmacy, Tehran University of Medical Sciences as a faculty member. He was promoted to full professorship in Pharmaceutics in 2005. He then became the Dean of the Faculty of Pharmacy at Tehran University of Medical Sciences in 2009 for 4 years.
Prof. Dinarvand has been active in the harmaceutical administration in both industry and government at the highest levels: seven years as CEO of several Pharmaceutical companies and twice as Deputy Minister of Health and Head of Iran Food and Drug Administration (8 years). He has also been involved in pharmacoeconomy and national drug policy research. However, his main research interest is in the area of nanomedicine and polymeric drug delivery systems and has published over 450 international papers in this field. In recent years he has focused on the design and application of nano-structures as targeted drug delivery systems mainly in the field of cancer treatment. His group have established several knowledge-based companies active in this field. He is the founder and director of Nanotechnology Research Centre, Tehran University of Medical Sciences.

Is-12: Checkpoint Adaption by Cyclin-Like Proteins Promotes Susceptibility for more Aggressive, Drug-Resistant Breast Tumours

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Senescence and quiescence are mechanisms used to maintain proper balance of cell populations and to protect cells from overgrowth or growth during unfavourable conditions. Overriding this protective event permits uncontrolled cell growth in cancer. At a molecular level senescence/quiescence is enforced through the inhibition of the cell cycle at well-established checkpoints. Healthy mammary cells overcome checkpoint arrest to re-enter the cell cycle and expand cell populations throughout development and during changing environmental conditions. Dissecting the reversibility of this checkpoint may reveal essential molecular mediators in the initiation and progression of cancer. Our lab has demonstrated that an atypical cyclin-like protein, Spy1 is capable of bypassing senescent and quiescent checkpoints throughout development, following DNA damage and during aging in a number of different cell types. Using transgenic mouse models we have established that elevated levels of this protein expands normal stem cell populations and renders the organism susceptible to breast, brain and liver cancers. Human patient data demonstrates that this protein is found at

elevated levels in each of these cancers. Manipulating levels in patient derived samples we demonstrate that even advanced tumours can be sensitized to chemotherapy approaches dependent upon cell cycle arrest. This presentation will describe a negative feedback loop between Spy1 and the tumour suppressor p53; whereby p53 keeps overall levels of the Spy1 protein in check. When elevated, Spy1 is capable of overriding the cell cycle and apoptotic effects of p53. In the face of DNA damage, damage will accumulate. Interestingly, in stem cell populations elevated levels of Spy1 promotes the reprogramming of cell populations to a more primitive state – even demonstrating hallmarks of pluripotency.
This presentation will also highlight the importance of understanding the role of these atypical proteins in driving breast cancer stem cells and contributing to the aggressiveness of disease. We find that reducing levels of this protein in human breast cancers reduces stemness properties and sensitizes breast cancers to select drug treatments. This presentation will focus on our data to date to discover the mechanism by which Spy1 aids in breast cancer stem cell expansion and drug resistance and to demonstrate a potential strategy by which we may target this pathway therapeutically.

Is-13: Harnessing The Potential of SATB Family Proteins as A Novel Molecular Target for Cancer Therapy Using Statins

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Colorectal cancer is the second leading cause of cancer-related deaths worldwide, highlighting the need for improved treatments and advanced molecular research. A recent therapeutic approach focuses on repurposing drugs to target dysregulated pathways involved in tumorigenesis. Among these, statins, commonly known for lowering cholesterol, have attracted attention for their potential anti-cancer properties. Here, we provide direct evidence for the same by assessing the impact of statin treatment on lipid, transcript, and protein levels. Our findings reveal that statins specifically target key components of the Wnt/β-catenin pathway, a major factor in adenoma formation, including the Special AT-rich Binding protein (SATB) family proteins. While SATB1 is recognized as a regulator of tumorigenesis, particularly under Wnt signaling, SATB2 appears to exert an opposing role. We demonstrate that statin treatment reciprocally alters the expression pattern of these proteins. Furthermore, a human clinical trial evaluating statins as an anticancer therapy supports the hypothesis that differential expression of SATB proteins is crucial in tumorigenic outcomes. In conclusion, this modulation by statin treatment suggests promising new therapeutic avenues through drug repurposing.

Is-14: Development of Adoptive NK Cell Therapy for Cancer Treatment

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Recently T cell therapy has been added to the standard treatment of cancer. CAR-T cells direct against CD19 or BCMA are being administered to patients suffering from hematological tumors. Although the clinical success is clear, it comes at the cost of serious side effects that need additional treatment to contain them. We have been aiming to develop adoptive Natural Killer cell therapy as due to their different activation mechanism they are expected to cause less (severe) side effects. Over the years we have developed a GMP compliant NK cell expansion protocol using feeder cell technology in which we can obtain 30-40 billion NK cells from a starting population of 10-20 million (present in 400 ml peripheral blood). These NK cells have a activated phenotype, including CD16 expression allowing for Antibody Dependent Cellular Cytotoxicity. We have shown in cell lines, mice, human cancer organoids and primary human tumor cells that these expanded NK cells have a powerful killing capacity. They can also be genetically modified (NKG2A knock-out or CAR introduced) and show an improved killing over unmodified NK cells.

Is-15: RNA-Mediated Epigenetic Attenuation of The Cell Senescence via Locus-Specific Induction of Endogenous SIRT1

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SIRT1, a known regulator of cellular senescence, is a therapeutic target for age related disorders and its upregulation is a strategy to improve the cell therapeutic potentials of human mesenchymal stem cell (MSCs). Knockdown of natural antisense transcripts via small activating RNAs (RNAa) is an emerging approach for safe and locus specific gene regulation. We have recently identified a natural antisense transcript at human SIRT1 locus (SIRT1-NAT), the expression of which shows a negative correlation with that of SIRT1. To test the hypothetic upregulation of SIRT1 via knockdown of SIRT1-NAT, in this study we designed a single stranded oligonucleotide (SIRT1-antagoNAT) against the antisense transcript, transfection of which efficiently knocked down the SIRT1-NAT and induced SIRT1 transcription in human MSCs. In addition, activation of SIRT1 transfection via knockdown of SIRT1-NAT in human MSCs enhanced their proliferation and differentiation potentials, reduced senescence associated β-galactosidase activity and reversed the senescence associated molecular alterations. Our findings introduce an RNAa mediated approach for epigenetic induction of endogenous SIRT1 and the consequent attenuation of senescence. Further studies should evaluate the therapeutic potentials of this approach against various age related disorders.

Is-16: Boost Brittle Bones Before Birth: A Clinical Trial on Stem Cell Transplantation for Treatment of Osteogenesis Imperfecta

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Objectives: Severe osteogenesis imperfecta (OI) can be diagnosed before birth. No efficient therapy is available for OI, but pre-clinical and initial clinical data show that mesenchymal stem cells (MSCs) could be used to ameliorate OI. BOOSTB4 is an open label phase I/II trial evaluate the safety and efficacy of postnatal or pre- and postnatal intravenous administration of first trimester human allogeneic fetal liver MSCs as a treatment of OI type 3 or severe type 4 with glycine substitutions in COL1A1/COL1A2.
Materials and Methods: The trial's primary endpoint is safety and tolerability of intravenous administration of MSCs to the infant and fetus, and safety for the pregnant woman. The secondary efficacy endpoints are fracture frequency, time to fracture, growth, bone mineral density, biochemical bone turnover and clinical OI status. Exploratory endpoints are quality of Life, paracrine and immune cell effects, and donor cell engraftment. The treatment groups are compared to matched historical controls (EudraCT-number: 2015-003669-60, ClinicalTrial.gov: NCT03706482).
Results: The trial is performed in Sweden (dosing and follow-up) and the Netherlands (follow-up) and includes children from 7 European countries. Each child received 4 doses at 4-month intervals. In total 67 postnatal doses and 3 prenatal doses have been administered to 18 children. The subjects underwent inpatient monitoring at each dose until 48 (dose 1–2) or 24 (dose 3–4) hours. Until the 12-month follow-up no significant short-term adverse reactions have been identified in the infant, pregnant woman or fetus. The last primary follow-up at 6 and 12 months after the last dose was performed mid-January 2024, and the efficacy will be evaluated under 2024. The subjects are followed yearly for 8 further years.
Conclusions: To date, the subjects have received all doses of MSCs with no short-term complications recorded. The primary follow-up until 12 months after the last dose has been performed, and the efficacy is now summarised. The BOOSTB4 project has received funding from the EU Horizon 2020 research and innovation programme (Grant No 681045), the Swedish Research Council and Region Stockholm.

Is-17: Industrial Development of Advanced Therapy Medicinal Products

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Advanced therapy medicinal products (ATMPs) are divided into four distinct types: GTMPs, SCTMPs, TEPs, and the combined ATMPs (cATMPs). GTMPs are products directly related to therapeutic, prophylactic, or diagnostic effects with a recombinant nucleic acid sequence. SCTMPs are products that contain substantially manipulated cells or tissues, or the cells or tissues not intended to be used for the same essential function(s) in the recipient and the donor. TEPs are engineered cells or tissues that have the properties of regenerating, repairing, or replacing human tissue, all in accordance with the medicinal products general definition and finally, cATMPs comprise another type of these products and contain one or several medical devices that are an integral part of the GTMPs, SCTMPs, or TEPs. For Industrial development of advanced therapy medicinal products with specific quality criteria, in compliance with all necessary regulatory requirement, a quality management system that includes quality assurance (QA) and quality control (QC) plan should be applied in all operations. The establishment and maintenance of a quality management system could assure the long- term sustainability of the mentioned products. Furthermore, quality systems are necessary for the delivery of high-quality products to the end-user. In this regard, some quality assurance and quality control activities are interrelated, the two are defined differently. Quality assurance is an integrated system of management activities involving planning, implementation, documentation, assessment, and improvement to ensure that quality is embedded in every step of the production. Quality control is the system of technical activities that measures the attributes and performance of a process or product against defined standards to verify that the stated requirements are fully met. An essential component of quality management is a formal system for documentation and record-keeping. The documents of the quality management system ensure that the industrial production infrastructure is in compliance with regulatory and safety requirements.

Is-18: Customizable Bone Composite Scaffold Incorporating Inductive Molecules: A Novel Approach

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Bone grafting, particularly after blood transfusion, is one of the most commonly performed procedures globally, driven by the need for bone volume enhancement in dental implant surgeries. Adequate bone regeneration is often necessary before implant placement, especially in the maxillary and mandibular regions. Techniques like the sausage technique, titanium mesh, non-absorbable membranes, and the use of autogenous, allogeneic, and xenogeneic bone blocks are common methods for augmenting jawbone height and width. However, addressing large defects, particularly within the jaw, often requires extensive surgical time and can lead to complications.
Recent advances in digital dentistry and molecular biology have revolutionized bone defect reconstruction. Customized bone grafts, designed from 3D images using CB-CT scans and DICOM files, offer a significant innovation in treatment. These grafts, traditionally made from allogeneic bones, are now being complemented by customized xenogenic and synthetic blocks, optimized through 3D printing and milling technologies.
The key benefits of using customized bone blocks include reduced surgical time, decreased morbidity, and improved accuracy in graft fitting. Computer-aided design and manufacturing (CAD/CAM) technology stands out by being applicable to a wide range of grafting materials, offering advantages over 3D printing. Designing these customized structures requires careful consideration of geometric and biological factors, including the patient's jawbone volume, systemic health, medications, and defect specifics.
Moreover, the integration of additive materials such as collagen, absorbable polymers, and inductive autogenous materials

like PRF (Platelet-Rich Fibrin) enhances graft success. These materials support healing by preventing soft tissue infiltration into hard tissue and providing necessary growth factors, ultimately contributing to the effectiveness of the bone grafting process.

Is-19: How to overcome the regulatory challenges of CAR T cell therapy?

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CAR T-cell therapy has become a promising treatment for cancer, especially for hematologic malignancies, with several FDA approvals. However, this cutting-edge cancer therapy faces some significant challenges and regulatory concerns. One of the primary challenges is the complexity of the manufacturing process. CAR T-cell therapy involves extracting T cells from a patient, genetically modifying them to express chimeric antigen receptors (CARs), and then expanding these modified cells before reinfusing them into the patient. Ensuring consistency and quality can be challenging due to the complex and multi-step process, which can result in product batch variations. Furthermore, the production and distribution logistics of these therapies are complicated and require specialized facilities and strict quality control procedures Another major challenge is managing the severe side effects associated with CAR T-cell therapy. Patients may develop neurotoxicity and cytokine release syndrome (CRS), which can be life-threatening if not treated properly. These side effects require close monitoring and immediate intervention, making treatment more complex.
The FDA has raised new concerns regarding the long-term safety of CAR T-cell therapies. Recent studies have highlighted the potential risk of secondary cancers developing following treatment. The genetic modification required to produce CAR T cells raises this concern because it can inadvertently lead to genetic changes that promote the development of new cancers. Due to this, the FDA now requires lifelong monitoring of patients treated with CAR T-cell therapies and has mandated boxed warnings to inform patients of this rare but serious risk.
Moreover, the high cost of CAR T-cell therapies represents a significant barrier to their widespread adoption. Due to the high cost of production and administration, many patients are unable to receive these therapies. The FDA regulatory framework offers detailed instructions for the creation, production, and clinical testing of CAR T-cell therapies in an effort to address these issues. However, ongoing updates and case-by-case assessments are necessary due to the quick advancements in this field, which frequently surpass the regulatory framework .
In summary, while CAR T-cell therapy offers promising benefits for cancer treatment, it also poses significant challenges in terms of manufacturing complexity, side effect management, long-term safety and cost. Ongoing efforts by international regulatory authorities to address these issues are critical to ensure the safe and effective implementation of these innovative therapies.

Is-20: Decoding Early Human Development with Blastoids

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One week after fertilization, human embryos undergo the critical process of implantation into the uterus, a fundamental event vital for both embryonic and adult life. However, the intricate nature of this process presents significant challenges for direct investigation. In our study, we elucidated how stem cells serve as a valuable tool for modeling early human development through the creation of blastoids. By culturing human pluripotent stem cells (hPSCs) in PXGL medium and inhibiting the Hippo, TGF-β, and ERK pathways, we successfully generated blastoids with an efficiency surpassing 70%. These blastoids faithfully represent the three lineages (trophectoderm, epiblast, and primitive endoderm). Blastoids spontaneously establish the first axis and show directional attachment capabilities to endometrial cells. Furthermore, they faithfully recapitulate the morphological and developmental trajectory of the blastocyst, generating transcriptionally accurate preimplantation-stage cells. As a reliable and efficient model, blastoids offer a viable and ethically sound alternative to the utilization of human embryos in the study of implantation and early development.

Is-21: The Potential Significance of Extracellular Vesicles in Osteoarthritis Treatment

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Osteoarthritis (OA) is the most prevalent rheumatic disease worldwide that leads to progressive articular cartilage destruction. Conventional therapies that include disease-modifying drugs and surgical interventions lack the capability to fully treat OA and regenerate functional articular cartilage. Although mesenchymal stem cell (MSC) therapy has been proposed to treat various degenerative diseases such as OA, abnormalities in cellular behaviors caused by in vitro cultures or donor characteristics, as well as undesired hypertrophy and ossification, limit their clinical use. Extracellular vesicles (EVs) are trophic factors secreted by various cell types in the extracellular environment that provide a novel therapeutic opportunity. The therapeutic effects of EVs have been identified as a significant factor in intercellular communication in different disease treatments, including OA. Compared to the conventional approaches in treating OA, EV therapy is a non-invasive and cell-free method. However, improving the yield of EVs and their therapeutic effects are the main challenges for clinical applications. In this talk, I will discuss EV engineering strategies in order to achieve an efficacious therapeutic outcome. The importance of co-culture engineering as an indirect EV engineering method that efficiently increases EV production and quality to achieve a more therapeutic effect for the restoration of cartilage defects with natural properties will be also covered.

Is-22: Engineering Tools to Interrogate the Host Immunity, Microbiome and Their Crosstalk

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The interplay between the commensal microbiota and the mammalian immune system development and function includes multifold interactions in homeostasis and disease. Nevertheless, many unknowns and challenges remain in disentangling microbiome-immunity interactions. Although animal models have been used extensively to analyze host-microbiome interactions and their contributions to pathophysiology, there are limited bioengineered systems available to recapitulate the complexity of the human organs and verify the host immune-microbiome interactions. Recent advances in tissue engineering, microfabrication and stem cell biology have enabled the development of more sophisticated systems, in particular organoid cultures and organ-on-chip microfluidic models, that can provide unparalleled independent control over biomechanical, biochemical, and cellular parameters, and faithfully recapitulate the cellular microenvironment and tissue function and advance personalized medicine. Such systems, along with recently emerged sampling microneedle approaches that enable the longitudinal, in situ immune monitoring of human patients, are great tools to identify the immune-microbiome interactions in different human conditions. Here, I highlight the human intestine chip we have developed to establish stable complex community of living human aerobic and anaerobic commensal gut microorganisms in direct contact with living, mucus producing human intestinal epithelium in vitro. In addition, I will explore the application of our developed sampling microneedle skin patch platform, which allows for noninvasive and longitudinal monitoring of immune responses in various scenarios. While there are currently limited advanced bioengineered methods exist to study the human complex host-microbiome crosstalk, I present novel concepts for harnessing these technologies to construct advanced models that effectively simulate and capture the complex dynamics of long-term host-microbiome interactions. We will use these engineered tools to further understand the mechanistic causal relationships between commensal microbiota and host innate and adaptive immune systems in infectious diseases, autoimmunity and cancer.

Is-23: AI in Healthcare: Bridging the Gap Between Innovation and Clinical Impact

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In this 15-minute talk, I will explore the transformative potential of AI in healthcare, focusing on its role in early disease detection, personalized medicine, and operational efficiency. The discussion will highlight how AI-driven tools are not just improving patient outcomes but are also enhancing the capabilities of healthcare professionals. Drawing on real-world examples, including Connectivity's cognitive assessment technology, I will address the challenges of integrating AI into clinical practice, such as data privacy, regulatory hurdles, and the need for robust clinical validation. The talk will conclude with a vision for the future, emphasizing the importance of collaboration between AI developers, clinicians, and policymakers to ensure that AI innovations translate into meaningful improvements in healthcare delivery.
Key Topics to Cover:
1. The Role of AI in Early Disease Detection: How AI is enhancing early diagnosis, with examples from brain health and other domains; The potential for AI to detect subtle changes that may be missed by traditional methods.
2. Personalized Medicine: AI's impact on tailoring treatments to individual patients; How AI models can analyze vast amounts of data to predict patient responses to therapies.
3. Operational Efficiency: AI applications in streamlining hospital operations, reducing errors, and optimizing resource allocation. Case studies on how AI is reducing the burden on healthcare providers.
4. Challenges and Opportunities: The importance of data privacy and security in AI healthcare applications; Navigating regulatory landscapes to bring AI innovations to market; The need for rigorous clinical validation to build trust and adoption among clinicians.
5. Future Outlook: The evolving role of AI in healthcare and its potential to democratize access to quality care.

Is-24: Transposon-Mediated Genetic Methods in Zebrafish and Their Applications to The Study of Neuroscience

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For the past decade, we have developed Tol2-transposon mediated genetic methods, including transgenesis, gene trapping, enhancer trapping and the Gal4FF- UAS system in the model vertebrate zebrafish. By using these methods, we have performed a large-scale genetic screen, and generated more than 2,000 transgenic lines that expressed Gal4FF, a synthetic Gal4 transcription activator, in specific cells, tissues, and organs. Further, we constructed a web-based database zTrap (https://ztrap.nig.ac.jp/ztrap/), in which transgenic fish can be searched based on their expression patterns and transposon integration sites. Thus, our transgenic fish resource has been powerful for the study of developmental biology, neuroscience, and disease modeling.
We have investigated functional neuronal circuits controlling the larval and adult behaviors by employing the transgenic fish resource. First, we aimed to disclose how visual stimuli evoke appetite during the larval prey capture behavior. By using brain-specific Gal4FF fish and the UAS:GCaMP effector fish, we successfully imaged the neuronal activity during prey capture in real-time. We found that the visual stimulus recognized by the optic tectum activates the hypothalamic feeding center through prey detector neurons in the pretectum. Second, we aimed to identify functional equivalents of the mammalian amygdala and hippocampus, that play crucial roles in processing emotional memory or episodic and spatial memory, respectively. We constructed fish carrying UAS:botulinum-neurotoxin gene, and inhibited the activity of various Gal4-expressing neurons in the brain. We found a neuronal population in Dm (dorsomedial telencephalon) is essential for fear conditioning in zebrafish, and a

neuronal population in Dl (dorsolateral telencephalon) is essential for the episodic (trace fear conditioning) and spatial learning. Thus, we propose these neuronal populations are functional equivalents of the amygdala and hippocampus in teleost.

Is-25: Impact of Culture Conditions on Cytokine Expression in Mesenchymal Stromal Cells: Implications for Regenerative Medicine

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Objective: Multipotent mesenchymal stromal cells (MSCs) have garnered significant interest in regenerative medicine due to their remarkable immunomodulatory properties and potential therapeutic applications across a spectrum of pathological conditions. Emerging evidence suggests that the efficacy of MSCs-based therapies is intricately linked to the cellular microenvironment, including the tissue source from which MSCs are derived and the culture conditions in which they are maintained. In this study, we aimed to compare secretome among MSCs derived from different sources and cultured in different conditions.
Materials and Methods: MSCs were isolated from diverse tissue sources, including adipose tissue (AT), bone marrow (BM), gingiva (G), placenta (PL), and umbilical cord (UC). These MSCs were cultured either as monolayers (2D) or cell spheroids (3D). Immunophenotype and osteogenic, chondrogenic, adipogenic differentiation potential were evaluated. Cytokines and growth factors in MSCs-conditioned media (CM) samples were analyzed utilizing xMAP technology (Luminex, USA).
Results: MSCs expressed the mesenchymal markers (CD105, CD73, CD90, CD44) and demonstrated trilineage differentiation capacities. Analysis of cytokine expression in MSCs-CM unveiled distinct cytokine profiles among MSCs derived from different sources and culture conditions. Notably, UC-MSCs-CM exhibited elevated levels of cytokines compared to CM from other MSC sources. Moreover, comparison between 2D and 3D cultures of UC-MSCs revealed differences in cytokine expression, with 3D cultures demonstrating higher levels. These findings emphasize the influence of culture conditions on the cytokine profile of MSCs.
Conclusion: The observed differences in cytokine expression highlight the importance of optimizing culture conditions for MSCs-based therapies. UC-MSCs, particularly from 3D cultures, show promise as a potent source of cytokines with potential applications in treating inflammatory and tissue repair disorders. Further research into the specific mechanisms underlying these cytokine differences and their therapeutic effects is warranted to harness the full potential of MSCs-based therapies. The study was supported by the Academic leadership program Priority 2030 proposed by Sechenov University.
Keywords: Conditioned Media, Cytokines, Mesenchymal Stromal Cells, Secretome, 3D Culture

Is-26: Synthesis of Cell-based Chronic Wound Dressing with Gelatin Methacrylate (GelMA) Hydrogel for Skin Regeneration

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Objective: Effective wound healing requires quick wound closure, less scarring, and accelerated angiogenesis. Hydrogels stand out among dressing materials and offer a number of benefits that promote wound healing because of their high biocompatibility, structural resemblance to the extracellular matrix (ECM), and highwater content. Despite the fact that hydrogel is frequently employed in tissue engineering, it is not the best option because of its weak mechanical and vascularization capabilities. Here, we coated GelMA hydrogel on silicone polymer. GelMA hydrogel mixed with amniotic membrane extract increased angiogenesis properties of the wound area.
Materials and Methods: A 1:1 mixture of pharmaceutical-grade two-component A&B silicone was prepared. It was then put into polymethyl methacrylate (PMMA) molds, heated for 5 minutes at 120 °C to form a silicone film. Pharmaceutical grade GelMA (10% concentration) was prepared, then 0.1 mg/ml amniotic membrane extract, Irgacure 2959 were added, the resulting solution was poured onto the silicone film and exposed to UV (at 365 nm) light for 1 minute. Structural tests including SEM and tensile test were carried out to prove the strength of the scaffold used. The amount of tube formation was examined in order to study the angiogenesis.
Results: The results of this study showed that the silicone structure has no pores and its surface is completely smooth and has no cracks in the structure. The GelMA 10% structure has suitable pores with a size of 65 micrometers. Biodegradability tests showed that the thin layer of GelMA starts to degrade and release the amniotic membrane extract at the wound site after 24 hours. The in vitro tests showed that the blood cells in the vicinity of the prepared dressing had a very good tube formation after 48 hours compared to the sterile gas control sample.
Conclusion: Because of the lengthy treatment times, delays in healing of chronic wounds, they have an impact on quality of life and on costs. Today, silicone wound dressings are widely used in the repair of chronic wounds. It can be concluded that skin tissue engineering using GelMA to the silicone surface and amniotic membrane extract can speed up the healing of wound while preventing exudate buildup and the formation of scar tissue.

Is-27: Will Be Announced

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Is-28: 3D Intestinal Organoid Platform to Test Epithelial Recovery Potential of Lead Bioactives

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We present a novel 3D intestinal organoid microarrayed high-throughput platform designed to assess the epithelial recovery potential of various lead bioactive compounds under conditions simulating intestinal barrier disruption. The platform leverages human- and canine-derived small intestinal organoids to model inflammatory conditions, such as those present in inflammatory bowel disease (IBD). Through the application of inflammatory challenges (e.g., CytoMix and IFN-γ), the system allows for real-time observation of barrier disruption and subsequent epithelial recovery. Recovery interventions with bioactives, such as NAD+ precursor and dexamethasone, were tested, showing differential effects on the restoration of barrier integrity. RNA sequencing in single-organoid resolution revealed the involvement of key signaling pathways, including WNT/β-catenin, in the recovery process. The platform's high-throughput capability, coupled with hallmark pathway analysis, enables precise quantification of bioactive efficacy, providing a robust tool for evaluating therapeutic potentials aimed at epithelial repair and recovery.

Is-29: Novel Micrornas Enabling The Maintenance and Derivation of Embryonic Stem Cells from Blastocysts

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Cells of the inner cell mass (ICM) acquire a unique ability for unlimited self-renewal during transition into embryonic stem cells (ESCs) in vitro, while preserving their natural multilineage differentiation potential. Several different pathways have been identified to play roles during ESC maintenance and derivation but the function of non-coding RNAs in this process is poorly understood. Here, we describe several microRNAs (miRNAs) that are crucial for the efficient maintenance and generation of mouse ESCs from ICMs. Using small-RNA sequencing, we identify critical miRNAs in cultured ESCs and characterize dynamic changes in miRNA expression profiles during ICM-ESC transition in a high-resolution, time-course dependent manner. We report several waves of miRNA transcription during ESC formation, to which miRNAs from the imprinted Dlk1-Dio3 locus contribute extensively. In silico analyses followed by functional investigations reveal that Dlk1-Dio3 locus-embedded miRNAs (miR-541-5p, miR-410-3p, and miR-381-3p), miR-183-5p, and miR-302b-3p promote, while miR-212-5p and let-7d-3p inhibit ESC formation. Moreover, the same miRNAs from the Dlk1-Dio3 locus promote the maintenance of the so-called ground-state ESCs by targeting differentiation-associated genes. Collectively, these findings offer new mechanistic insights into the role of miRNAs in ESC maintenance and during ESC derivation.
Keywords: microRNA, pluripotency, stemness, early embryo, ES cells

Is-30: Artificial Intelligence Biology and Reciprocal Disruption

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Advances in artificial intelligence (AI) and biology are frequently highlighted in both scientific and popular media, as each field has significantly impacted our lives. However, the future holds even greater potential due to the emerging reciprocal disruption between AI and biology. Disruption in the biological side roots in using AI tools for biological experiment automation and implicit modeling of biological systems, in addition to hypothesis generation and testing. Interestingly, the opposite direction is also originated in AI, where we have faced high energy consumption of silicon intelligence at scale, need for big data, complexity of learning tools, and most importantly have remained behind solo-AI. These limitations have triggered research in Bio-AI and Neuro-AI where we seek biological and social solutions to overcome the current limitations of AI toward creation of artificial general AI.

Is-31: Prefrontal Control of Visual Signals

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Visual attention is an integral part of our daily life. A network of cortical and subcortical structures are involved in control of visual attention. To date, how these areas interact with each other and the chain of events giving rise to visual attention are still unclear. I will present our findings regarding the neurons and neuromodulators involved in attention and will discuss how these findings help us untangle the neural circuitry of attention.

Is-32: Do *In Vitro* Fabricated Cardiac Microtissues Replace Experimental Models in Cardiovascular Research?

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The current knowledge on the cardiovascular biology and pathology was mostly obtained by using animal models. However, there are considerable interspecies differences which hinder the application of results for human. Therefore, the two-dimensional (2D) culture systems of human cardiovascular cells intervened, in order to resolve these difference. While, conventional 2D cultures proved effective in studying cardiac function using both primary culture as well as human pluripotent stem cell-derived cardiovascular lineage cells, these systems exhibit inherent limitations such as lack of three-dimensional (3D) cell-cell and cell-extracellular matrix interaction. To address these challenges, tissue engineering technology offered the integration of biomaterials as substrates alongside cardiac lineage cells, thus creating an environment more suitable to conduct precise in vitro cardiovascular research. Natural and synthetic biomaterials were employed to establish scaffolds, forming a 3D platform for generating heart microtissue. Today, simultaneous applica-

tion of electromechanical stimulation as well as biochemical cues considerably improved the formation of a cardiac tissue-like platform for related studies. These platforms were verified with respect to structure and function in order to be used as alternatives of animal models for cardiovascular research. However, there are some challenges remaining such as appropriate vascularization and incorporation of immune cells in order to mimic the native cardiac microenvironment. These challenges are being carefully investigated and will be the priority for the next few years.

Key words: Cardiac Microtissue, *In Vitro* 3D Culture, 2D Culture

Is-33: Stem Cell-Based Human Embryo Models

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Modelling early human embryogenesis with naïve pluripotent stem cells. In early mammalian embryos, cells with identical genomes exhibit distinct gene expression patterns. In addition, human embryo development leads to the formation of complex structures by day 14 of development. Development relies on precisely orchestrated gene regulatory programs and epigenetic processes that determine cell identity and tissue architecture. The tight control of gene expression is critical throughout an organism's lifetime. In this talk, I will present our efforts to understand the role of chromatin regulators in early human development and pluripotency. In addition, I will explore the regulation of gene dosage, using X-chromosome dosage compensation as a paradigm. I will present novel data challenging existing notions about mammalian dosage compensation regulation. Additionally, I will also discuss recent advances achieved using human naïve pluripotent stem cells to model the initial two weeks of human development, including emerging stem cell-based embryo models. I will discuss how these advances revolutionize the way we study developmental epigenetics.

Is-34: Early-Stage Brain Stem Cell Therapy for Treating Progressive Multiple Sclerosis

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Advances in stem cell biology have raised great expectations that diseases of the central nervous system may be ameliorated by the development of non-hematopoietic stem cell medicines. Yet, the application of stem cells as therapeutics is challenging and the interpretation of some of the outcomes ambiguous. The initial idea that stem cell transplants work only via structural cell replacement has been challenged by the observation of consistent intercellular information exchange between the graft and the host. Sustained stem cell graft-to-host exchange of signals has led to remarkable trophic effects on endogenous brain cells and beneficial modulatory actions on innate and adaptive immune responses that ultimately promote the healing of the injured CNS. Among a few promising candidate stem cell sources, neural stem/precursor cells (NSCs) are being extensively investigated for their capacities to signal to the immune system upon transplantation in experimental CNS diseases.

The rationale for NSC therapeutics efficacy studies in people with progressive MS is based on (i) our progress in developing cell isolation and expansion technologies 1,2; on (ii) the successful demonstration of the effectiveness of syngeneic and xenogeneic NSC grafts in a variety of transplant models of MS-like disease and lesions in small rodents and non-human primates 3-6; and (iii) the completion of the first and largest phase I clinical trial employing allogeneic, single donor, hNSC-based ACTs from a homogeneous cell source in people with SPMS paving the way for the administration of the same standardized stem cell medicinal product in future clinical trials of efficacy 7. Here I will discuss new mechanisms of cellular licensing by which transplanted NSCs counteract CNS-compartmentalised chronic inflammation in mice and potentially also in humans. By understanding the mechanisms of intercellular (neuro-immune) signalling, chronic diseases of the brain and spinal cord that include progressive MS may be treated more effectively, and significant neuroprotection and restoration of key functions may be achieved with new tailored molecular therapeutics.

Is-35: The Pantetheinase VNN1 Regulates Energy Metabolism in Acute Myeloid Leukemia Stem Cells By Controlling The Availability of Coenzyme A

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To enhance the clinical outcomes for patients with acute myeloid leukemia (AML), targeting leukemic stem cells (LSCs) is essential. These cells are at the top of the cellular hierarchy and are the main cause of disease relapse. LSCs mainly use oxidative phosphorylation (OXPHOS) and fatty acid oxidation (FAO) to meet their energy needs, both of which depend on coenzyme A (CoA). Our study shows that the enzyme pantetheinase Vanin1 (VNN1) is crucial for maintaining LSCs. VNN1 is more abundant in LSCs than AML blasts and healthy hematopoietic stem and progenitor cells (HSPCs). Genetic and pharmacologic interventions revealed that VNN1 is necessary for LSC function but not for healthy HSPCs. Inhibiting VNN1 specifically targets immature leukemic cells, and high VNN1 expression is a strong predictor of poor prognosis in AMLs with primitive cellular structures. Mechanistically, reducing VNN1 levels or inhibiting its activity lowers intracellular CoA levels, leading to a shift from OXPHOS and FAO to lactate production. This change makes cells more sensitive to BCL-2 inhibition by Venetoclax. Our findings suggest that targeting the VNN1-CoA pathway could effectively disrupt LSC function, especially in some AML subtypes, and when combined withVenetoclax.

Is-36: The Evolution of Human Blastocyst Development and Implantation

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Embryogenesis is the vehicle of evolution through which genetic variations turn into heritable innovations. Human embryos differ from those of primates in their implantation strategy, exhibiting deep but fragile uterine invasion. Our laboratory has developed an embryo model known as the blastoid, which is unique in two ways: it is complete and represents the pre-implantation stage, enabling the modelling of implantation in utero. Here, we leveraged the versatility and throughput of blastoids to study the genetic properties underlying a specific features of primate clades, namely superficial and deep invasion. We used single-cell RNA and ATACseq data to reconstruct the GRN of human tissue that mediates invasion, identified essential TFs that were validated by genetic knockout in blastoids and subsequent in vitroattachment and invasion assays. Using deep learning and convolutional neural networks based on transfer learning, we identified enhancer sequences and DNA motifs that regulate these TFs. Using a comparative approach, we pinpointed clade-specific differences in enhancers that correlate with phenotypes. This functional exploration reveals aspects of genome evolution that have impacted early human embryogenesis.

Is-37: Blastoids: Modeling Blastocyst Genesis and Implantation with Stem Cells.

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The blastocyst is the early mammalian organism before implantation inthe uterus. We have promoted the self-organization of stem cells intomodels of mouse and human blastocysts, which we have namedblastoids (Nature 2018, Nature 2021). Blastoids are morphologically andtranscriptionally similar to the blastocyst and contain analogs of all threecell types that would eventually develop into the complete organism(embryonic and extraembryonic). Because blastoids are complete andmodel the preimplantation stage, they can be introduced into the uterus(mouse model) or combined in vitro with uterine cells (human model) to recapitulate aspects of the normally hidden implantation processes. Unlike blastocysts, blastoids come in large numbers and facilitate a more systematic modulation and analysis of development. As such, they represent both a scientific and ethical alternative to the use of embryos for research. Using this approach, we are investigating the genome evolution underlying species-specific aspects of blastocyst development and implantation, with the long-term goal of understanding the evolutionary basis of suboptimal human pregnancy (50% of fertilized eggs never develop). This knowledge could help solve the global health problems of family planning and developmental origin of health and disease.

Is-38: Electrically Conductive Biohybrid Hydrogels for Maturing hiPSC-Derived Cardiomyocytes and Protecting The MI-Heart Against Arrhythmia

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Introduction: Myocardial infarction (MI) causes cell death, disrupts electrical activity, triggers arrhythmia, and results in heart failure, whereby 50-60% of MI patients die from sudden cardiac death (SCD). Due to a limited renewal capacity of adult cardiomyocytes the MI-induced cardiomyocyte loss proceeds to the formation of fibrotic tissue and subsequent ventricular wall dilation. The fibrotic tissue is electrically insulating, and such a low conductivity, together with hetero-cellular interactions in the scar border zone, contribute to electrical decoupling of the remaining viable cardiomyocytes in the infarcted region, thereby promoting asynchronous ventricular contractions. The most effective therapy for SCD prevention is implantable cardioverter defibrillators (ICDs). However, ICDs contribute to adverse remodeling and disease progression and do not prevent arrhythmia. Moreover, there is a gap in designing an electrically conductive hydrogel that prevents post-MI arrhythmia and has the potential to be combined with cardiomyocytes. We developed an injectable collagen-PEDOT:PSS hydrogel that protects infarcted hearts against ventricular tachycardia (VT) and can be combined with hiPSC- cardiomyocytes to promote partial cardiac remuscularization.
Materials and Methods: We have generated an injectable collagen-PEDOT:PSS hydrogel and studied gelation kinetics, electrical conductivity as well as the hydrogel micromorphology by scanning electron microscopy. Moreover, we generated engineered cardiac tissues based on hiPSC-derived cardiomyocytes and these hydrogels and studied cell survival, microcellular organization of contractile machinery and calcium handling of these cells in the tissues for them up to 40 days. Moreover, RNA-sequencing analyses revealed a shift towards more mature cardiomyocytes within electrically conductive hydrogels without any external stimuli. Eventually we have transplanted the hydrogels in a cryoinfarction model of MI in mouse. We have assigned five groups, including sham, MI, collagen, collagen-PEDOT:PSS, and collagen-PEDOT:PSS containing hiPSC-derived cardiomyocytes.
Results: PEDOT:PSS improves collagen gel formation and results in a faster gelation. It transforms single-fibrillar collagen morphology into entangled thick helical microfibrous morphology in collagen-PEDOT:PSS and increases electrical conductivity from ~41 mS/cm for collagen to ~65 mS/cm for collagen-PEDOT:PSS. Compared to cells in collagen hydrogels, hiPSC- cardiomyocytes in collagen-PEDOT:PSS hydrogels exhibit near-adult sarcomeric length (~2 μm), improved contractility (~500%), enhanced calcium handling, and conduction velocity (~700%). RNA-sequencing data revealed an upregulation of genes associated with conduction, structure, energetics, oxidative phosphorylation and fatty acid oxidation, calcium handling, and cell-ECM interactions, indicating enhanced maturation and improved cell-matrix interactions in hiPSC- cardiomyocytes within collagen-PEDOT:PSS hydrogels. Injecting collagen-PEDOT:PSS hydrogels in infarcted mouse hearts results in a ~400% decrease in ventricular tachycardia occurrence compared to MI, reaching to the levels of healthy hearts. Furthermore, hiPSC-cardiomyocyte implementation results in improved heart function (fraction shortening: 25% vs. ~18% in MI).
Conclusion: Collectively, the here-developed hydrogel showed great potential to promote stem cell derived cardiomyocyte maturation and to protect the infarcted heart against ventricular tachycardia. Finally, collagen-PEDOT:PSS hydrogels offer a versatile platform for treating injuries in hearts and other electrically sensitive tissues.

Is-39: Mechanisms of Embryo Failure at Implantation

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Aneuploidy, the presence of an abnormal number of chromosomes, is a major cause of early pregnancy loss in humans. Yet, the developmental consequences of specific aneuploidies remain unexplored. We have explored the extent of post-implantation development of human embryos bearing common aneuploidies using a recently established culture platform. We have seen that while trisomy 15 and trisomy 21 embryos develop similarly to euploid embryos, monosomy 21 embryos exhibit high rates of developmental arrest, and trisomy 16 embryos display a hypo-proliferation of the trophoblast, the tissue that forms the placenta. Using human trophoblast stem cells, we show that this phenotype can be mechanistically ascribed to increased levels of the cell adhesion protein E-CADHERIN, which lead to premature differentiation and cell cycle arrest. We identify three cases of mosaicism in embryos diagnosed as full aneuploid by pre- implantation genetic testing. Our results present the first detailed analysis of post-implantation development of aneuploid human embryos.

Is-40: Mitochondria-Incorporated Electroconductive Alginate-Based Hydrogel

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Background Here, the angiogenesis properties of mesenchymal stem cell (MSC) mitochondria were investigated in a rat model of myocardial infarction. Material and Methods Mesenchymal stem cells were pre-treated with mitochondria-induction compounds metformin (Met; 50 μM), and dichloroacetic acid (DCA; 40 μM). After the isolation of mitochondria, the isolated particles were characterized and incorporated (~2 × 107 particles) inside the alginate (3%)-gelatin (1%) hydrogel containing 1 μM pyrrole in the presence of FeCl3. The physicochemical properties of the final composite were monitored using several assays such as FTIR, swelling, biodegradation, porosity tests, and SEM. Mitochondria-loaded hydrogels (~2 × 107 particles/100 μl) were injected into the border zone of infarcted myocardium induced by LAD ligation. After two weeks, rats were euthanized and mitochondrial uptake and angiogenesis status were monitored using histological examination. Results Data showed appropriate physicochemical (swelling rate, biodegradation, porosity) and cytocompatibility properties of alginate-gelatin pyrrole hydrogel evaluated by SEM, FTIR, and MTT assays. Flow cytometry analysis indicated high-rate purity and functionality of isolated mitochondria. Masson's Trichrome staining and ECG analysis indicated appropriate myocardial infarction in the control rats. Immunohistochemistry analysis showed the stimulation of angiogenesis in the infarcted area (vWF+ capillaries↑, and α-SMA+ arterioles↑) in rats that received mitochondria-loaded hydrogel compared to mitochondria and hydrogel groups ($P<0.05$). Data showed a significant increase in anterior wall thickness in the mitochondria-loaded hydrogel group ($P<0.05$). Conclusion Mitochondria-loaded hydrogels are suitable delivery platforms for the induction of angiogenesis and reduction of fibrosis in ischemic myocardium.
Keywords: Mesenchymal Stem Cells, Mitochondria, Electroconductive Alginate-Gelatin/Pyrrole Hydrogel, Rat Myocardial Infarction, Angiogenesis

Is-41: Dissecting The Molecular Mechanisms of Mammalian Germline Development Using Single Cell Omics Sequencing Approach

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Meiotic recombination is initiated by programmed DNA double-strand breaks (DSBs). Limited by the scarcity of fetal germ cells, the dynamics and epigenetic regulatory mechanisms of meiotic DSBs in females remain elusive. We generate the genome-wide map of mouse female DSBs at single-cell resolution. The number and high dynamic range of meiotic DSBs in individual cells rewrite previous perceptions. We prove that the sequence-specific binding of PRDM9 directly induces chromatin remodeling rather than a permissive environment around DSBs that had been created in advance. Our study covers multiple histone modifications and reveals their unique enrichment patterns and regulatory functions during DSB formation. Our results comprehensively elucidated the distribution and epigenetic regulation of meiotic DSBs in female mammals.

Is-42: Bioprinting of the made-to-order organs

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Background: The area of personalized organ fabrication is highly important in the fields of healthcare and biotechnology, providing groundbreaking solutions for challenges in organ transplantation, personalized medicine, and the management of diverse health conditions. Bioprinting is a leading-edge technology in organ engineering, presenting novel prospects in this field. The current work summarizes recent developments, challenges, and future prospects in bioprinting for personalized organ production.
Results: To ensure successful tissue production, scaffolds must mimic the specific microenvironment necessary for cell spreading, proliferation, and differentiation. The microarchitecture of the scaffold should correspond to the mechanical signals required by cells, depending on the type of tissue. Laser-based

techniques like two-photon polymerization (2PP) offer a wide range of materials for creating customized scaffolds that resemble native tissue structures, guiding cell behavior. Bioprinting methods are crucial for precise cell distribution within scaffolds, with techniques like Laser-Induced Forward Transfer (LIFT) enabling high-resolution manipulation of cells. Spheroids, the units of future tissues, can be organized into specific patterns. Extrusion bioprinting has enabled the creation of complex bioequivalents on a larger scale, specifically with spheroids, gaining traction as ideal building blocks due to their regenerative potential, physiological mimicry, and self-organizing abilities, surpassing traditional 2D cultures and cell suspensions in efficacy.

Conclusion: While significant advancements have been achieved in bioprinting technologies in recent years, each approach has its own set of constraints, such as limitations in process resolution, scalability, and the availability of compatible bioinks. Nevertheless, current progress suggests that the strengths of different methods can offset their respective weaknesses. In the future, it is probable that technologies will merge various modalities into unified platforms, incorporating innovative techniques like cell aggregate bioprinting. This integration aims to address existing technological gaps and produce tissue constructs that are scalable, structurally sound, perfusable, and exhibit enhanced biomimicry and desired functionality. The study was supported by the Russian Science Foundation (№23-15-00481).

Key words: Bioprinting, Tissue Engineering, Scaffolds, Regenerative Medicine

Is-43: Potential of Freeze Dried-Secretome From Human Wharton's Jelly Mesenchymal Stem Cells for Wound Healing

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Background: Burn injury, caused by heat, chemicals, electricity, radiation, or friction, can rapidly disrupt body homeostasis, leading to multi-organ dysfunction and potentially life-threatening injuries. Indonesia has a high incidence of burn injuries, leading to the development of new therapies for non-healing wounds. Among the most promising is stem-cell-based therapy. The secretome from human Wharton's Jelly Mesenchymal Stem Cells (hWJMSCs-Sec) offers diverse biological activities that are particularly beneficial for skin applications and wound healing, making it a key alternative in regenerative medicine. Research objective: The research investigates the application of freeze-dried and freeze-dried gel from hWJMSCs-Sec on burn injured-rats by analyzing protein expression.

Materials and Methods: Male rats were subjected to burn injuries using an instrument probe applied to the dorsal area for 10 seconds. After burn induction, freeze-dried and gel freeze-dried hWJMSCs-Sec were applied to the dorsal area once or twice daily for 16 days. Epidermal protein expression of Interleukin-1β (IL-1β), Transforming Growth Factor-β (TGF-β), Keratinocyte Growth Factor (KGF), and Collagen (COL) was measured using Immunohistochemistry (IHC). Additionally, gene expression of Epidermal Growth Factor (EGF), Tissue Inhibitor of Metalloproteinases-1 (TIMP-1), Matrix Metalloproteinase-1 (MMP-1), and COL-1A1 was analyzed using quantitative Real-Time Polymerase Chain Reaction (qRT-PCR). Epidermal inflammation and angiogenesis were assessed using Hematoxylin-Eosin (HE) staining.

Results: On day 16, during the proliferation phase of wound healing, treatment with freeze-dried and freeze-dried gel from hWJMSCs-Sec improved wound healing by reducing IL-1β and enhancing TGF-β, KGF, and COL expression. Additionally, during the proliferation phase, these treatments increased the epidermal gene expression of EGF, TIMP-1, MMP-1, and COL-1A1. Furthermore, freeze-dried and freeze-dried gel from hWJMSCs-Sec treatments also improved inflammation and angiogenesis during the proliferation phase of wound healing. Conclusions: Freeze dried- and freeze-dried gel from hWJMSCs could improve and accelerate wound healing process.

Is-44: Ipscs-Derived Venous Endothelial Cells for Modeling Vascular Malformation and Drug Discovery

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Venous malformations (VMs) represent prevalent vascular anomalies typically attributed to non-inherited somatic mutations occurring within venous endothelial cells (VECs). The lack of robust disease models for VMs impeded the discovery of new drugs. Here, we implemented heterozygous mutation into iPSCs and devised a robust protocol for the generation of iVECs. This protocol involved the deliberate manipulation of cell cycle dynamics mediated through the retinoid signaling pathway. The mutated iVECs exhibited aberrant TIE2 signaling and formed dilated blood vessels *in vivo*, thereby recapitulating the phenotypic characteristics observed in VMs. Moreover, utilizing a deep neural network and a high-throughput DRUG-Seq approach, we performed drug screening and identified Bosutinib that effectively rescued the disease phenotype in vitro and *in vivo*. In summary, by leveraging on the genome editing and stem cell technology, we generated VM models that enabled the development of new potential therapeutics.

Is-45: Design and Development of Nano Formulated Bioacteve Component for Molecular Targeted Therapy of Cancer Stem Cells

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The development of targeted treatments for cancer and cancer stem cells (CSCs) is crucial in overcoming the challenges of recurrence and resistance to conventional treatments. This research focuses on the design and development of a nano-delivering system for a bioactive compound that targets CSCs specifically. Using nanotechnology, the bioactive component was encapsulated in a nano-delivering system to increase its stability, bioavailability, and precise targeting of CSCs. The nanoformed compound was evaluated by in vitro and *in vivo* studies to assess its efficacy in inhibiting CSC growth and disrupting the major molecular pathways involved in their self-renewal and survival. The results indicate that this nanodispersion system significantly improves the therapeutic impact of the bioactive compound, reducing the effectiveness of the CSC and overcoming chemoresistance. This innovative approach highlights the potential of combining bioactive compounds with nanosystems to target cancer therapy. By providing a new method for targeting CSCs, this research contributes to ongoing efforts to develop more effective cancer treatments and pave the way for clinical applications aimed at reducing tumor recurrence and improving patient outcomes.

Is-46: Wnt Signaling in Stem Cell Differentiation and Tissue Regeneration

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Wnt family members are secreted-type glycoproteins that orchestrate major developmental processes in the embryonic state and regulate maintenance, self-renewal and differentiation of adult mammalian tissue stem cells. Wnt/β-catenin pathway has been recently identified as one of the key players in neuronal differentiation. We showed that during trabecular meshwork-derived mesenchymal stem cells (TM-MSCs) differentiation into neuron-like cells, β-catenin protein accumulation was increased in the nucleus, indicating the increased activity of Wnt/β-catenin pathway in the time-window of neuronal differentiation. Interestingly, DKK1 transcript level was reduced dramatically in TM-MSCs during this differentiation period. In consistent with the above results, treatment of neurally induced TM-MSC with CHIR (Wnt agonist) significantly elevated the expression level of neuronal markers while treatment with IWP-2 significantly decreased these markers. These results suggest that the neuronal fate in TM-MSCs is triggered specifically by Wnt/β-catenin activation and attenuated if it is antagonized. There are also increasing evidence that Wnt/β-catenin pathway is a key regulator of neural tissue regeneration. To address this question, we fabricated an electrospun nanofibrous scaffold (ENS) containing polylactide nanofibers and lithium ion (Li) as a Wnt/β-catenin signaling activator. Our results showed that the Li loaded ENSs gradually released Li during 11 days of culture, with the range concentration that upregulate the expression of Wnt/β-catenin target genes. Moreover, the expression levels of Schwann cell markers in human adipose-derived mesenchymal stem cells (hADMSCs) cultured on these scaffolds, were notably increased compared to those in the control. Our *in vivo* assay showed that implantation of Li loaded ENSs (with or without cells) in the rat model of crush injury improved behavioral features and electrophysiological parametres and also increased number of organized regenerating axons of injured sciatic nerve. From our results, it can be implied that Li is the main element of our fabricated scaffold contributing to sciatic nerve regeneration. Li may exert its effect by activating Wnt/β-catenin signaling pathway emphasizing the role of this signaling pathway in neural differentiation and regeneration.

Keywords: Wnt/β-catenin Signaling, Neuronal Differentiation, Regeneration, Nanofibrous Scaffold

Is-47: Human Retinal Organoids for Disease Modeling

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With the significant advances in human stem cell biology and organoid medicine, currently in vitro differentiation of human retinal organoids is well established. In this talk, I will introduce its application for disease modeling for retinitis pigmentosa and retinoblastoma.

Oral Presentation

Os-1: Establishment of Bladder Patient Derived Tumor Organoid for Drug Screening

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Objective: Bladder cancer (BLCa) is one of the most cost-intensive cancers with a poor prognosis due to high recurrence. Thus, there is an urgent need for unique preclinical models recapitulating patient-specific histopathological and molecular diversity that patients could benefit from a more personalized treatment approaches. To address this need we established bladder cancer organoid as an advanced organ culture model for predicting drug response which indicate the inter-patient heterogeneity.
Materials and Methods: In our study, we establish patient derived tumor organoid cultures from different muscle-invasive and non-muscle-invasive BLCa stages and grades. The tumor organoids were characterized based on culture efficacy, gene and protein expression by RT-PCR and immunofluorescence microscopy. PDOs preserve the histological and molecular heterogeneity of the parental tumors. Drug screening pipeline is implemented using PDOs, tested standard-of-care (cisplatin & gemcitabine) and FDA-approved compound (lapatinib) for other tumors.
Results: The tumor organoids showed high expression of CK14 (Basal marker) and LGR5, other genes (CK14, CK20, LGR5, UPK III, FOX1A, GATA3a, CK5 and CK44) didn't show significance difference in expression. Quantification of IF imaging showed 3D structure of tumoroid with high expression of KI67, CK20, β-actin, and UPK III. Drug screening showed the combination of cisplatin and lapatinib significantly decreased the viability of PDO.
Conclusion: By further assessing the pathological results and clinical history of cases, we determined that monitoring of tumor-drug responses via bladder organoid model has the potential to determine and optimize patient-specific treatment efficacy.
Keywords: Bladder, Drug Screening, Personalized Medicine, Tumor Organoid

Os-2: Impact of Culture Conditions on Cytokine Expression in Mesenchymal Stromal Cells: Implications for Regenerative Medicine

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Objective: Multipotent mesenchymal stromal cells (MSCs) have garnered significant interest in regenerative medicine due to their remarkable immunomodulatory properties and potential therapeutic applications across a spectrum of pathological conditions. Emerging evidence suggests that the efficacy of MSCs-based therapies is intricately linked to the cellular microenvironment, including the tissue source from which MSCs are derived and the culture conditions in which they are maintained. In this study, we aimed to compare secretome among MSCs derived from different sources and cultured in different conditions.
Materials and Methods: MSCs were isolated from diverse tissue sources, including adipose tissue (AT), bone marrow (BM), gingiva (G), placenta (PL), and umbilical cord (UC). These MSCs were cultured either as monolayers (2D) or cell spheroids (3D). Immunophenotype and osteogenic, chondrogenic, adipogenic differentiation potential were evaluated. Cytokines and growth factors in MSCs-conditioned media (CM) samples were analyzed utilizing xMAP technology (Luminex, USA).
Results: MSCs expressed the mesenchymal markers (CD105, CD73, CD90, CD44) and demonstrated trilineage differentiation capacities. Analysis of cytokine expression in MSCs-CM unveiled distinct cytokine profiles among MSCs derived from different sources and culture conditions. Notably, UC-MSCs-CM exhibited elevated levels of cytokines compared to CM from other MSC sources. Moreover, comparison between 2D and 3D cultures of UC-MSCs revealed differences in cytokine expression, with 3D cultures demonstrating higher levels. These findings emphasize the influence of culture conditions on the cytokine profile of MSCs.
Conclusion: The observed differences in cytokine expression highlight the importance of optimizing culture conditions for MSCs-based therapies. UC-MSCs, particularly from 3D cultures, show promise as a potent source of cytokines with potential applications in treating inflammatory and tissue repair disorders. Further research into the specific mechanisms underlying these cytokine differences and their therapeutic effects is warranted to harness the full potential of MSCs-based therapies. The study was supported by the Academic leadership program Priority 2030 proposed by Sechenov University.
Keywords: Conditioned Media, Cytokines, Mesenchymal Stromal Cells, Secretome, 3D Culture

Os-3: Wnt/Beta-Catenin Signaling Regulates Osteoblast Dedifferentiation During Zebrafish Bone Regeneration

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Objective: Cellular dedifferentiation is an important phenomenon that is invoked to form source cells for regeneration in various vertebrate species and organs. We define dedifferentiation as the process by which a differentiated cell reverts back to a less differentiated state and becomes proliferation-competent. In response to fin amputation, osteoblasts (OB) proximal to the amputation plane start to dedifferentiate, become proliferative and migrate to form part of the regeneration blastema. In zebrafish, only retinoic acid and NF-κB signaling have been de-

scribed as regulators of OB dedifferentiation. Our aim here is to better characterize the molecular changes occurring in dedifferentiating osteoblasts.

Materials and Methods: We have performed 10X Genomics Single cell RNA and Bulk RNA sequencing experiments at different timepoints by FAC-sorting OBs of all lineages using Zns5 antibody, and mature OBs only using a bglapl:eGFP reporter line respectively. For global inhibition of Wnt signaling pathway we used a hs:Axin1-YFP transgenic line, and for manipulating this pathway in epidermis and fibroblasts we used Cre-lox approach.

Results: We found that OBs are very heterogenous during de- and re-differentiation, and we discovered two trajectories where mature OBs and mesenchymal cells are major source of regeneration. Mechanistically, we found that Wnt/beta-catenin pathway is positively enriched within dedifferentiated OBs. Intriguingly, we found that ectopic Wnt signaling inhibition reduced OB dedifferentiation, and its inhibition in epidermis enhances, and in fibroblasts impairs dedifferentiation.

Conclusion: While our and other labs have described important roles for Wnt signaling at later stages of fin regeneration, including in OB re-differentiation, a potential function in the regulation of OB dedifferentiation has not been uncovered. Thus, it would be interesting to investigate Wnt signaling pathway regulation of OB dedifferentiation in more detail by finding targets and regulatory networks, and also delving deeper into the OB heterogeneity and interaction with other cells.

Keywords: Zebrafish Fin Regeneration, Wnt/Beta-Catenin Signaling, Single Cell RNA Sequencing, Intrinsic Regeneration, Cellular Dedifferentiation

Poster Presentations

Ps-1: Targeting Glioblastoma Stem Cells: A Comparative Study of NK Cell Cytotoxicity

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Objective: Glioblastoma (GBM), a prevalent primary malignant brain tumor, poses significant treatment challenges. One such challenge is the presence of cancer stem cells (CSCs) that exhibit resistance to chemotherapy and radiotherapy. The quest for advanced therapies to counter these cells has given rise to therapies based on immune cells. The selective transfer of immune cells, particularly Natural Killer (NK) cells, offers substantial therapeutic potential against tumor cells. Over the past decades, two-dimensional (2D) tumor models have been employed to study the efficacy of immune cell cytotoxicity. However, these 2D models lack structural complexity and fail to simulate the physiological conditions of the tumor microenvironment. Consequently, the effectiveness of immune cells against tumor cells, as demonstrated in these models, may not fully translate into clinical studies. To gain a more profound understanding of tumor-immune cell interactions, spheroid tumor models, which are more physiologically relevant, have been developed. These spheroid models can simulate dynamic cellular activities, thereby providing a more accurate representation of *in vivo* tumor profiles and cancer stem-like cells. Here, we aimed to investigate the cytotoxicity of NK cells in glioblastoma cancer stem-like cells (GCSLC) of the U251 GBM cell line in comparison to traditional 2D models.
Materials and Methods: Spheroid-forming assay in a serum-free culture medium was used to enrich the cellular population with stem-like properties. Spheroids were characterized by evaluating the stemness markers and clonogenicity. Moreover, spheroid and 2D models were co-cultured with NK cells and cytotoxicity was analysed using flow cytometry.
Results: Our findings, obtained through immunophenotyping, revealed that the expression of CSC markers in the spheroid model surpasses that in the 2D model. Furthermore, we evaluated the cytotoxicity of primary human NK cells, both activated with interleukin-15 and inactive, against these two models using flow cytometry. Our findings indicate that both inactive and activated NK cells exhibit higher cytotoxicity against 2D models compared to spheroid models.
Conclusion: Our study concludes that spheroids exhibit resistance to the cytotoxicity of NK cells activated with interleukin-15.
Keywords: Cancer Stem Cells, Glioblastoma, NK cells, Spheroid Culture, 2D Culture

Ps-2: Evaluation of NANOG Gene Suppression and Replacement of Let-7 in Breast Cancer Cell Line and The Effects on Stemness, Invasion and Apoptosis of Cells

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Objective: Failure and recurrence in breast cancer (BC) treatment because a significant obstacle in cancer therapy, and identification of cell population named cancer stem cells (CSCs) in the tumor can be help us to define these cells as target in novel therapeutic strategy. The goal of this research is to find a correlation between stemness and metastatic characteristics, to address whether CSCs are a potential target of therapy because of its developmental behavior and similarities with normal stem cells. Here, we focus on the expression of NANOG in breast CSCs, a key molecule in the physiological process of stem cells. Abnormally alteration in the miRNAs expression such as Let-7a has been demonstrated in several cancers, including BC.
Materials and Methods: SKBR3 cells have transfected by NANOG siRNA and Let-7a miRNA mimic by electroporation. Then, we have evaluated the effects of NANOG inhibition and the increase Let-7a on the apoptosis, invasion, migration, and stemness feature of the cells. Results: Our results showed that the inhibition of NANOG coincided with Let-7a increase contribute to significant decrease in stemness feature. The invasion factors such as MMP9 showed the low levels (2.8-fold) of invasion rate after transfection the cells. The apoptosis rate of the SKBR3 cells increased after transfection (35%) compared to control cells. As well as the increase in the BAX/BCL2 ratio (6-fold) confirmed the flow cytometery analysis of apoptosis. According to the results, the difference between the siRNA and miRNA mimic groups was not significant, but the differences between transfected cells with the control cells were significant.
Results: Our data showed the importance of Let-7a and Nanog in cancer progression. In conclusion, these findings showed that a combination of Let-7a miRNA mimic and Nanog siRNA could be exploited as a new treatment to enhance tumoricidal strategy treatment and to improve the cancer therapy outcome.
Conclusion: In this study, we showed that the using a combination of Let-7a increase and NANOG inhibition could possibly tumoricidal outcome.
Keywords: Breast Cancer, Let-7, NANOG

Ps-3: Harnessing The Power: Prenatal Decellularization for Tissue Repair

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Objective: The practice of prenatal decellularization has emerged as a promising avenue in regenerative medicine, with a specific focus on harnessing the unique capabilities of the placenta. This innovative approach involves the meticulous removal of cellular components from the placental tissue while preserving its extracellular matrix architecture and bioactive factors. By

unlocking the regenerative potential of decellularized placental scaffolds, we aimed to pave the way for revolutionary advancements in tissue engineering, organ transplantation, and wound healing therapies.
Materials and Methods: In the current study, the decellularized placenta powder was obtained using detergents such as sodium dodecyl sulfate and triton, finally it was freeze dried. *In vitro* characterization including total protein content, DNA content, and histology staining was deeply conducted. Furthermore, the biocompatibility of the prepared powder on fibroblast cell viability was investigated.
Results: This study delves into the innovative methods used to create decellularized scaffold powder, a versatile biomaterial that provides a structural framework for cell growth and tissue regeneration. According to our result, the decellularized scaffold showed retained extracellular matrix after decellularization, efficient retained extracellular matrix, and excellent biocompatibility *in vitro*.
Conclusion: Altogether, this study delves into the intricacies of harnessing the power of placenta decellularization, shedding light on its current applications, challenges, and future prospects in the realm of regenerative medicine.
Keywords: Perinatal, Placenta, Regenerative Medicine, Scaffold

Ps-4: Preparation and *In Vitro* Anticancer Evaluation of Etoposide Encapsulated Niosome Nanocarriers

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Objective: In today's world, nanomedicine-based therapeutics are used to treat breast cancer as the leading cause of death in females. Etoposide (ETO) is used in treatment of many malignancies including breast cancer, but its hydrophobicity cause hinderance to achieve high drug loading. Niosomes are novel drug delivery systems forms by self-assembly of nonionic amphiphiles in aqueous media. The aim of present study was to develop a drug delivery system based on niosome to encapsulate the ETO and investigate the safety and effectiveness of the newly developed system.
Materials and Methods: Introduced niosome has been prepared by thin layer hydration method. Particle size and zeta potential were evaluated using dynamic light scattering (DLS), and drug release rate from the system was investigated *in vitro*. Safety of the DDS and its gradient was checked using bone marrow mesenchymal stem cells (BMSCs) and red blood cells (RBC). MDA-MB-231 cell line was used to check the DDS+ DXR and CXR only.
Results: The newly formulated Niosome system NI showed excellent stability for up to 3 months at 4°C. The particle size was reported to be approximately 399.37 nm and its poly dispersity index (PDI) was 0.4. In addition, the drug loading rate was 89% and the releasing percentage of the drug after 24 hours through mouse skin and dialysis membrane was obtained as 37 and 52 %, respectively. The half maximal inhibition concentration (IC 50) of the drug for 48 and 72 hours of treatment was calculated to be 33.26 and 31.49 µg/ml respectively.
Conclusion: The newly developed NI-ETO system is suitable drug delivery system based on its high drug carrier capacity, releasing rate and its medicine safety.
Keywords: Breast Cancer, Drug Delivery, Etoposide, Niosome

Ps-5: Nebulization of Mesenchymal Stem Cells Secretome Attenuates Acute Respiratory Distress Syndrome Caused by SARS-CoV-2 Corona Virus

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Objective: Indeed, mesenchymal stem cells (MSCs) have shown promise in treating COVID-19 patients due to their immunomodulatory, anti-inflammatory, and regenerative properties. However, the limited lifespan of transplanted MSCs poses a challenge. Utilizing the secretome of MSCs, which comprises various bioactive factors such as cytokines, growth factors, and extracellular vesicles, presents a promising alternative. These factors collectively contribute to tissue repair and regeneration, making them valuable in combating the inflammatory response and tissue damage associated with COVID-19. Harnessing the therapeutic potential of MSC secretome could offer a more sustainable and effective treatment strategy for COVID-19 patients.
Materials and Methods: The randomized clinical trial conducted in Kerman, Iran, aimed to assess the efficacy of nebulized concentrated MSCs secretome as an additional therapy for severe COVID-19 pneumonia. Twenty patients in the severe phase of COVID-19 pneumonia were randomly assigned to either the investigation group (received standard therapy plus nebulized concentrated MSCs secretome) or the control group (received standard therapy alone). The investigation group received 2 mL of nebulized concentrated MSCs secretome twice daily for five consecutive days in addition to standard therapy. The study evaluated several parameters to assess the effect of MSCs secretome therapy, including the length of stay in the intensive care unit (ICU), oximetry readings, and paraclinical results. These parameters were assessed at baseline and 5 days after ICU admission to determine any improvements or differences between the investigation and control groups. This trial aimed to provide insights into the potential benefits of MSCs secretome therapy as an adjunctive treatment for severe COVID-19 pneumonia, with the goal of improving patient outcomes and reducing the duration of ICU stay.
Results: The study findings indicate that nebulized concentrated MSCs secretome therapy, administered as an adjunctive treatment for severe COVID-19 pneumonia, led to favorable outcomes without any observed adverse effects. Patients who received MSCs secretome exhibited a significant decrease in ICU stay duration compared to those who received standard therapy alone (10.9 ± 3.75 vs. 5.5 ± 1.64 days, P=0.04). Additionally, the MSCs secretome-treated group showed significant improvement in O2 saturation (60.65 ± 16.58 vs. 79.47 ± 15.36, P=0.02) compared to the control group. Furthermore, during the study period, the investigation group demonstrated significant decreases in C-reactive protein (CRP), prothrombin time (PTT), and international normalized ratio (INR), along with an upregulation in the lymphocyte fraction (P<0.05 for all). These findings suggest that nebulized concentrated MSCs secretome therapy may have immunomodulatory and anti-inflammatory effects, leading to improved clinical outcomes and potentially reducing the severity of COVID-19 pneumonia.

Conclusion: The results of this preliminary study highlight the potential benefits and safety of using MSCs secretome as a therapeutic option for COVID-19 patients. However, further validation of these findings through additional clinical trials across different stages of the disease is strongly recommended. This will help to confirm the efficacy and safety of MSCs secretome therapy and provide more comprehensive evidence for its use in managing COVID-19.

Keywords: COVID-19, Hospitalization, Mesenchymal Stem Cells, Oximetry, Secretome

Ps-6: Evaluating The Anticancer Effects of 5-Fluorouracil and Aspirin Combination Against Gastric Cancer Cell Line

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Objective: Gastric cancer (GC) is one of the cancers that is diagnosed in advanced stages and mostly causes death. The prevention of drug resistance in malignancies has been significantly improved by combination therapy. However, the significant obstacle for therapeutic medications appears to be an increase in drug resistance. In the present study, 5-fluorouracil (5-FU) and aspirin were investigated as a combination therapy in a gastric cancer cell line (MKN) to overcome 5-FU drug resistance.
Materials and Methods: The combined effects of 5-fluorouracil (5-FU) and aspirin at various concentrations on cell viability and proliferation of MKN cells were assessed using the MTT assay after 48 h. Additionally, apoptosis was investigated by evaluating the expression of *Bcl-2* and *Casp3* genes using real-time *RT-PCR*. The results of the MTT assay and real-time RT-PCR were evaluated using graph pad prism software.
Results: Aspirin showed an IC_{50} value of 3 mM in MKN cells, while 5-FU showed an IC_{50} value of 80 µM. The combined IC_{50} values of aspirin and 5-FU were 2.5 mM and 60 µM respectively. The real-time polymerase chain reaction (PCR) analysis revealed an upregulation of *Casp3* expression and a downregulation of *Bcl-2* expression.
Conclusion: In conclusion, the current research demonstrated that the combination of aspirin and 5-FU concurrently induced apoptosis, inhibited cell proliferation, and decreased drug resistance in gastric cancer cell line.

Keywords: Aspirin, Drug Resistance, Gastric Cancer, 5-Fluorouracil

Ps-7: Correlation between Sperm and DNA Damage and Severe Asthenozoospermia in Men: An In-Depth Investigation

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Objective: Sperm motility is vital for successful fertilization, as it enables the sperm to penetrate the oocyte. Asthenozoospermia, defined by sperm motility under 42%, is a common cause of male infertility. This retrospective cohort study investigates sperm DNA damage using the TUNEL and SCSA methods, and explores its correlation with sperm parameters, age, and body mass index (BMI) in individuals with severe asthenozoospermia (motility less than two percent) compared to those with normozoospermia.
Materials and Methods: The study involved 111 individuals with severe asthenozoospermia and 113 individuals with normozoospermia. Sperm parameters were evaluated according to the World Health Organization's 2010 guidelines, while TUNEL and SCSA methods were used to assess sperm DNA damage. Statistical analysis included the t-test for two independent samples, and Pearson's correlation coefficient to examine the relationship between sperm DNA damage and sperm parameters, age, and BMI. Significance was considered at a level of $P>0.05$.
Results: Subjects with severe asthenospermia exhibited significantly lower average seminal fluid volume, sperm concentration, total sperm count, overall sperm motility, and progressive sperm motility compared to those with normal asthenospermia ($P<0.001$). Additionally, the average percentage of sperm DNA fragmentation was significantly higher in individuals with severe asthenospermia compared to normozoospermic individuals ($P<0.001$). A positive and significant correlation was observed between the extent of sperm DNA fragmentation and the age of men with severe asthenozoospermia.
Conclusion: Sperm motility, sperm DNA fragmentation, and paternal age are all critical factors that influence successful conception, fetal development, and offspring health. Therefore, the evaluation of sperm DNA fragmentation is recommended as part of male fertility assessments, as it can help guide the selection of appropriate treatment approaches for men with severe asthenospermia.

Keywords: SCSA, Sperm DNA Damage, Sperm Parameters, TUNEL

Ps-8: Enriched Human Embryonic Stem Cells-Derived CD133+, CD24+ Renal Progenitors Engraft and Restore Function in A Gentamicin-Induced Kidney Injury in Mice

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Objective: Acute kidney injury (AKI) is a common health problem that leads to high morbidity and potential mortality. The failure of conventional treatments to improve forms of this condition highlights the need for innovative and effective treatment approaches. Regenerative therapies with Renal Progenitor Cells (RPCs) have been proposed as a promising new strategy. A growing body of evidence suggests that progenitor cells dif-

ferentiated from different sources, including human embryonic stem cells (hESCs), can effectively treat AKI.
Materials and Methods: We describe a method for generating RPCs and directed human embryoid bodies (EBs) towards $CD133^+$ $CD24^+$ renal progenitor cells and evaluate their functional activity in alleviating AKI.
Results: The obtained results show that hESCs-derived $CD133^+$ $CD24^+$ RPCs can engraft into damaged renal tubules and restore renal function and structure in mice with gentamicin-induced kidney injury, and significantly decrease blood urea nitrogen levels, suppress oxidative stress and inflammation, and attenuate histopathological disturbances, including tubular necrosis, tubular dilation, urinary casts, and interstitial fibrosis.
Conclusion: The results suggest that RPCs have a promising regenerative potential in improving renal disease and can lay the foundation for future cell therapy and disease modeling.
Keywords: $CD133^+$, $CD24^+$, Embryonic Stem Cells, Kidney Injury, Renal Progenitors

Ps-9: The Effect of Platelet-Rich Plasma Injection on Decreases of Apoptosis of Multiple Sclerosis in Cuprizone Induced Model in Rats

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Objective: Multiple sclerosis (MS) is one of the most common neurodegenerative diseases in which the myelin shath. Although apoptosis of oligodendrocytes and neurons has been observed in MS lesions, the contribution of this cell death process to disease pathogenesis remains controversial. Platelet-rich plasma (PRP) is a blood derivative that has Decreases inflammatory and Apoptosis cell-regenerating properties. It also contains various cytokines and growth factors that may be beneficial for healing. The purpose of this research is the effect of platelet-rich plasma injection on inhibition of apoptosis of multiple sclerosis in cuprizone-induced model in rats.
Materials and Methods: The demyelination model was induced using an oral regimen of cuprizon 0/2 for 6 weeks. After that, blood was obtained from Royan stem cells company and after centrifugation, PRP was injected into mic. Extension demyelination and Rmyelination investigated were evaluated luxel fast Blue (LFB). Also in order to movement changes of BBB and footprint was investigated.
Results: PRP significantly reduced demyelination in tissues prepared using LFB and reduced the resulting cellular damage. In addition, PRP significantly improved the status of BBB and Foot print motor tests and appeared to inhibit induced apoptosis.
Conclusion: The results of this study show that PRP significantly increased myelin repair, reduced apoptosis through neuroprotective properties, and improved motor dysfunction.
Keywords: Apoptosis, Cuprizon, Multiple Sclerosis, PRP

Ps-10: The Effect of Umbilical Cord Blood Serum on Improving Liver Fibrosis in Rats

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Objective: Liver fibrosis is a serious condition that affects liver function and can be caused by various factors. Treatment usually involves anti-inflammatory drugs, but there is no complete cure yet. Umbilical cord serum contains growth factors and cytokines that can be beneficial for tissue regeneration and cell culture techniques.
Materials and Methods: The present study involved the establishment of an animal model using male Wistar rats by injecting CCl4 for 7 weeks to induce liver fibrosis. Subsequently, the umbilical cord blood serum was injected into the rats every day for two weeks intraperitoneally. Finally, after sacrifice, blood and liver tissue samples were collected. The final evaluation of the results included measuring the serum levels of ALT, ALP, and AST as well as histological tests using H&E and Masson's trichrome staining. Furthermore, gene expression changes are assessed using RT-PCR and statistical analysis is conducted using ANOVA.
Results: The serum levels of ALT, ALP, and AST showed a notable decrease, indicating a reduction in liver damage. Histological analysis revealed a decrease in fibrotic tissue and an improvement in liver architecture. Gene expression analysis showed a downregulation of fibrosis related genes. Statistical analysis confirmed the significance of these findings.
Conclusion: This study suggests that umbilical cord blood serum, improved liver function and reduced fibrotic tissue in a rat model of liver fibrosis. The results showed a decrease in liver enzymes, improved liver histology, and downregulation of fibrosis-related genes, indicating potential therapeutic benefits. Further research and clinical trials are needed to confirm these findings.
Keywords: Liver Dysfunction, Liver Regenerations, Umbilical Cord

Ps-11: Anti-Proliferative Activity of JQ for Melanoma and Underlying Mechanism

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Objective: Aggressive cancers such as melanoma have a high mortality rate and a high degree of resistance to conventional therapies. Inhibitors targeting growth factor receptors, which are frequently overexpressed and associated with melanoma progression, are among the intriguing new options for targeted therapy against this malignancy that have recently emerged. The lack of success of targeted therapy alone has led us to investigate the efficacy of treatment *in vitro* models with an bromodomain and extra-terminal domain (BET) inhibitor, JQ1.
Materials and Methods: Given their respective mechanisms of actions, we hypothesized the effect assessed by viability assay MTT could be due to the target genes affected. Hence the target genes in corresponding mechanism were characterized for their

expression by qRT-PCR in the A375 cell line to prove the effect of JQ1. For this purpose, different concentrations of JQ1 (10 nmol/mL - 2 Umol/mL) were tested and ERBB2, BRAF, CDKN2A, MITF and P38 evaluated to find the mechanism of action.
Results: As a result, we found the 2 μM of JQ1 can inhibit proliferation significantly in 48hr of treatment, A375 cells were treated by DMSO taken as control. Besides, treated cells with 2 μM of JQ1 showed significantly downregulated the CDKN2a (P16).
Conclusion: JQ1 inhibits proliferation and results in selective gene regulation. Effects of JQ1 suggesting its potential suitability as an anti-cancer drug targeting BRD4-mediated transcriptional regulation.
Keywords: Bromodomain-Containing 4 Inhibitor, Drug Screening, Melanoma, Small Molecule, JQ1

Ps-12: Angiogenic Properties of An Antimicrobial Lithium Chloride-Loaded Silk Fibroin/Alginate 3D Porous Scaffold for Promoting Diabetic Wound Healing: *In Vitro* and *In Vivo*

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Objective: Healing diabetic ulcers with chronic inflammation is a major challenge for researchers and professionals, necessitating new strategies.
Materials and Methods: To rapidly treat diabetic wounds in rat models, we have fabricated a composite scaffold composed of alginate (Alg) and silk fibroin (SF) as a wound dressing that is laden with molecules of lithium chloride (LC). The physicochemical, bioactivity, and biocompatibility properties of Alg-SF-LC scaffolds were investigated in contrast to those of Alg, SF, and Alg-SF ones. Afterward, full-thickness wounds were ulcerated in diabetic rats in order to evaluate the capacity of LC-laden scaffolds to regenerate skin.
Results: The characterization findings demonstrated that the composite scaffolds possessed favorable antibacterial properties, cell compatibility, high swelling, controlled degradability, and good uniformity in the interconnected pore microstructure. Additionally, in terms of wound contraction, re-epithelialization, and angiogenesis improvement, LC-laden scaffolds revealed better performance in diabetic wound healing than the other groups.
Conclusion: This research indicates that utilizing lithium chloride molecules loaded in biological materials supports the best diabetic ulcers regeneration *in vivo*, produces a skin replacement with a cellular structure comparable to native skin.
Keywords: Alginate, Angiogenesis, Diabetic Wound, Lithium Chloride, Silk Fibroin

Ps-13: Photobiomodulation Stimulates the Survivability of 3D Bioprinted MSC-Based Spheroids

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Objective: The emerging field of tissue engineering and 3D bioprinting necessitates innovative methods to enhance cell survival, proliferation, and differentiation. Photobiomodulation emerges as a promising approach due to its non-invasive nature, ability to penetrate highly hydrated structures, and demonstrated capacity to modulate cell physiology under stress conditions. This study aimed to evaluate the impact of photobiomodulation on mesenchymal stromal cells (MSCs) spheroids within 3D environments.
Materials and Methods: Mesenchymal stromal cells (MSCs) sourced from human gingiva were utilized to form spheroids. Photobiomodulation in the red (633 nm) and near-infrared (840 nm) spectra was administered using nonmonochromatic LED emitters (IPT RAS, Russia). A 3D cell culture was established using a hydrogel based on modified fibrinogen фтв пудфешт, and 3D bioprinted constructs were created with the CellInk Bio X 3D bioprinter (CellInk, USA). Cell physiology analysis encompassed cell viability assessment (Live/Dead staining), metabolic activity evaluation (AlamarBlue assay, ATP assay), proliferation rate determination (PicoGreen assay), ICC, and morphometric analysis.
Results: The bioprinting process was observed to impact cell viability. Both types of photobiomodulation were found to stimulate proliferative activity. Specifically, photobiomodulation at 840 nm wavelength was noted to enhance metabolic activity and ATP synthesis. Moreover, 3D printed structures exposed to near-infrared photobiomodulation exhibited slightly increased spheroid activity in terms of cell migration.
Conclusion: Conclusively, this study demonstrates the potential of photobiomodulation in promoting cell metabolic activity and proliferation within 3D tissue-engineered structures, suggesting new avenues for applying photobiomodulation in the field of bioprinting. The study was supported by Russian Science Foundation (№22-75-10120)
Keywords: Bioprinting, MSCs, Photobiomodulation, Spheroids

Ps-14: Preparation of Solid Lipid Nanoparticles Containing Docorubicin Using Microemulsion Method and Investigating Its Effect on Cancer Cells

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Objective: Doxorubicin (DOX), one of the most effective anticancer drugs frequently is used in breast cancer treatment. However, its clinical use is restricted by toxicity to normal cells and its low specificity against cancer cells. As an alternative, nanoparticle drug delivery systems such as Solid Lipid nanoparticles (SLN) is used to overcome these limitations in cancer therapy. This work is intended to develop and evaluate a SLN system that can efficiently load and release DOX and enhance its efficacy against MDA-MB-231 cancer cell line.
Materials and Methods: The SLN drug delivery system has been prepared by a new strategy based on microemulsion sys-

tem. Particle size and zeta potential were evaluated using dynamic light scattering (DLS), and drug release rate from the system was investigated *in vivo* and *in vitro*. Safety of the DDS and its gradient was checked using bone marrow mesenchymal stem cells (BMSCs) and red blood cells (RBC). MDA-MB-231 cell line was used to check the DDS+ DXR and CXR only.
Results: The particle size was reported to be approximately 145 nm and its poly dispersity index (PDI) was 0.238. It was observed that the system and its components are completely non-toxic. In addition, the drug loading rate was 93% and the releasing percentage of the drug after 24 h through mouse skin and dialysis membrane was obtained as 38 and 56 %, respectively. The half maximal inhibition concentration (IC_{50}) of the drug for 48 and 72 hours of treatment was calculated to be 1.19 and 0.94 µM respectively.
Conclusion: Safeness, drug carrier capacity and its releasing rate of the newly developed SLN showed that this system is a suitable carrier for doxorubicin.
Keywords: Cancer, Doxorubicin, Solid Lipid Nanoparticles, Targeted Drug Delivery

Ps-15: Mesenchymal Stem Cells Derived Exosome Transfected as a Therapeutic Vehicle for Mir-486 as a Novel Complementary Treatment for Glioblastoma

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Objective: Mesenchymal stem cells (MSCs) are integral components of the most essential reservoir of mature stem cells that facilitate tissue regeneration in both physiological and pathological contexts. Exosomes, small extracellular vesicles with diameters of 40–150 nm, are discharged through the fusion of multivesicular bodies with the plasma membrane. Exosomes originating from MSCs possess notable benefits such as enhanced stability, diminished immunogenicity, favorable biocompatibility, prolonged circulation duration, and a homing mechanism resembling that of Mesenchymal stem cells. MSC-exosomes have the potential to serve as suitable vehicles for delivering bioactive compounds or therapeutic agents in order to modulate the extracellular milieu and impact cancer pathophysiology for the purpose of treating tumors safely. MicroRNAs (miRNA) are a class of non-coding RNAs that significantly contribute to gene regulation. Exosomes released externally contain numerous miRNAs, enabling their transfer between cells through exosome release and absorption, thereby facilitating intercellular gene regulation. The impact of MSCs is closely linked to the significant release of exosomes containing functional miRNAs. Recent studies have shown MSC-exosomes carrying miRNA can enter tumor cells, alter miRNA levels, impact pathways, affect tumor progression, and contribute to tumor therapy. miRNAs have reportedly been demonstrated to be capable of being transferred into MSC-exosomes via electroporation. Moreover, it has been observed that the membrane of MSC-exosomes has the ability to generate transient pores by means of short electrical pulses. These pores facilitate the entry of miRNAs into MSC-exosomes. Glioblastomas (GBM), the most aggressive primary brain tumors, often exhibit poor responses to existing treatments. Numerous studies have demonstrated the potential of individual microRNAs in inhibiting angiogenesis, migration, and metastasis in glioblastoma. Many studies have illustrated that the predominant mechanism of resistance to Temozolomide (TMZ) is attributed to the overexpression of O6-methylguanine-DNA methyltransferase (MGMT).
Materials and Methods: In the course of our investigation, we carried out an exhaustive examination of data and studies in this particular area, employing data analysis tools to guide our research. Through this method, we were able to acquire a thorough comprehension of the topic and establish a robust basis for our investigation, guaranteeing that our conclusions are well-supported and based on current scientific insights.
Results: The expression profiles of miRNA in recurrent glioblastoma a significant reduction in the levels of miR-486-3p. The identification of O6-methylguanine-DNA methyltransferase as a direct target of miR-486-3p has been established, and it has been observed that reduced levels of miR-486-3p lead to an increase in the protein translation of MGMT.
Conclusion: Overall, MSCs driven exosomes can be an attractive therapeutic vehicles for miR-486 which have great potential to act as supplements to chemotherapy in the clinic.
Keywords: Exosome, Glioblastoma, Mesenchymal Stem Cells, MicroRNA

Ps-16: A Novel Protocol for Generation of Off-The-Shelf Growth Factor-Enriched Lyophilized Platelet-Rich Fibrin (Ly- PRF)

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Objective: PRF is a novel biological product containing growth factors and anti-inflammatory cytokines, suitable for inflammation regulation in regenerative medicine. In order to increase the growth factor and cytokine concentrations in the obtained product, we tried to optimize the centrifugation process. Moreover, to maintain the functionality of the product during the cryopreservation process, different storage procedures were applied and compared based on the functionality of the product.
Materials and Methods: Peripheral blood samples were isolated from four volunteers after obtaining their informed consent and thereafter, were centrifuged to form PRF. Different centrifugation speeds and temperatures were utilized in this step to figure out the optimum procedure. Moreover, different storage groups were considered to evaluate the impact of storage items on the functionality of the product. In this regard, one group was immediately lyophilized and stored in a -80°C freezer, one group was stored in a -80°C freezer and then, was lyophilized, and the third group was sorted in 4°C after lyophilization. Bradford assay and ELISA technique were used to assess the quantity and release of PDGF-BB, TGF-β, and VEGF in freshly prepared or long-term stored Ly-PRF samples at four different time points of 1, 24, 48, and 72 hours. Finally, the effect of our different groups on the tube formation capacity of endothelial and the polarization of macrophages was assessed.
Results: Bradford and ELISA results showed that all three assessed growth factors were highly enriched in all our groups although the fresh samples had higher amounts compared to the long-term stored samples (not significant). Moreover, time-dependent release of growth factors was observed in all groups.

Furthermore, freshly prepared Ly-PRF samples could significantly increase the tube formation capacity of endothelial and the polarization of macrophages compared to the stored Ly-PRF samples although the stored samples could also show angiogenic and anti-inflammatory properties.
Conclusion: Taken together, we tried to optimize the Ly-PRF generation procedure to obtain highly growth factor-enriched products. Moreover, we showed that although the long-term storage could affect the amount and functionality of proteins in Ly-PRF samples, the cryopreserved samples still had angiogenic and immune-modulatory properties, which could be utilized as off-the-shelf biological products in regenerative medicine.
Keywords: Growth Factors, Platelet-Rich Fibrin, Regenerative Medicine, Storage

Ps-17: Chick Embryo Extract Enhances Proliferation and Glial Differentiation of Dental Pulp Stem Cells for Neurodegenerative Therapy

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Objective: Dental pulp stem cells (DPSCs) are promising candidates for cell-based therapies in neurodegenerative diseases due to their ability to differentiate into neural lineages. However, their clinical application is hindered by limitations such as the need for extensive ex vivo expansion to achieve adequate stem cell numbers and efficient differentiation into neural lineages. This study aims to investigate the impact of chick embryo extract (CEE) preconditioning on the characteristics of DPSCs during *in vitro* culture.
Materials and Methods: DPSCs were isolated from the pulp region of rat teeth and cultured in a growth medium supplemented with either 10% fetal bovine serum (FBS) alone (control group, CTRL) or 10% FBS plus 10% CEE. Stem cell proliferation was assessed in both experimental groups after the first subculture by counting the cells and at passage 4 using the MTT assay. The mesenchymal stem cell identity of the DPSCs was confirmed at passage 4 through flow cytometry analysis of CD44 and CD90 markers. Additionally, the expression of genes related to stemness, neuronal, and glial differentiation was evaluated in both groups using real-time polymerase chain reaction (PCR).
Results: Our results demonstrated that CEE supplementation enhances the proliferation rate of DPSCs. Furthermore, CEE-treated stem cells expressed the mesenchymal markers CD44 and CD90 similarly to the CTRL group. However, CEE preconditioning significantly downregulated the expression of Nestin, a neural crest stem cell marker. The expression of neuronal markers BIII tubulin and MAP2 significantly decreased in CEE-treated stem cells, whereas the expression of the glial marker PDGFR-alpha increased.
Conclusion: These findings suggest that CEE preconditioning can confer desirable characteristics to DPSCs during *in vitro* culture, potentially enhancing their therapeutic application. Specifically, CEE preconditioning promotes stem cell proliferation, facilitating the production of sufficient stem cells for future transplantation, and biases the differentiation of these stem cells towards a glial lineage.
Keywords: Dental Pulp Stem Cells, Glial Marker, Preconditioning, Proliferation

Ps-18: Evaluating The Potential of Exosome-Encapsulated MicroRNA 149-3p in Developing Novel Endometriosis Therapy

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Objective: Endometriosis, as a chronic inflammatory disease brings remarkable social, public health, and financial consequences. Based on two theories of retrograde menstruation and stem cells, menstrual blood-derived stem cells (MenSCs) play a significant role in endometriosis since key genes of critical cellular processes are differentially expressed in MenSCs of endometriosis (E-MenSCs) and non-endometriosis women (NE-MenSCs). Since microRNAs (miRNAs) can regulate gene expression, we find the proper miRNA and assay its effects on modulating reactive oxygen species (ROS) and the gene expression level of inflammatory factors of E-MenSCs using NE-MenSCs-derived exosomes as the miRNA carriers.
Materials and Methods: After using publicly accessible algorithm-based databases, in Silico selection of miRNA regulating the most number of upregulated genes during endometriosis was done. E- and NE-MenSCs were cultured as controls, and the other experimental groups were as follows: E-MenSCs transfect with empty and miRNA vectors (E-MenSC+BB and E-MenSC+miR), and E-MenSCs treat with exosomes derived from non-transfected and miRNA-transfected NE-MenSCs (E-MenSC+Exo and E-MenSC+T-Exo). Then, the ROS amount and the expression level of interleukin (IL)-6, -8, -10 and 1β was evaluated through Elisa and real-time polymerase chain reaction (PCR), respectively.
Results: We found that ROS level was significantly lower in the E-MenSCs+ Exo and E-MenSCs+T-Exo group compared to the E-MenSCs. In addition, there was a significant increase in the gene expression levels of IL-6, -8, -10, and 1β in E-MenSCs compared to the NE-MenSCs. Although both E-MenSCs+T-Exo and E-MenSC+miR showed decreased IL-6, -8, and -10, none had decreased IL-1β level.
Conclusion: Since exosome-encapsulated mir-149-3p showed better modulating effects on E-MenSCs, the potential of exosomes as miRNA carriers could be considered in developing novel endometriosis therapies.
Keywords: Endometriosis, Exosome, Mesenchymal Stem Cells, Menstrual Blood, MicroRNA-149-3p

Ps-19: The Effects of Resveratrol on The Migration and Progression Ability of Menstrual Derived-Stem Cells in Endometriosis Patients

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Objective: Ten percent of women who are of reproductive age experience endometriosis, an inflammatory gynecological and hormone-dependent disease. Owing to the deficiencies of current therapeutic approaches, it is imperative to utilize novel additional, and alternative medications to improve endometriosis treatments. Due to its numerous biological actions, such as antineoplastic, anti-oxidant, anti-angiogenic, anti-proliferative, anti-inflammatory, and pro-apoptotic properties, resveratrol, a phytochemical, received a lot of attention. It has been demonstrated that the gene expression profile of menstrual blood-derived stem cells (MenSCs) differs between endometriosis and non-endometriosis women, supporting two theories regarding the pathophysiology of endometriosis: retrograde menstruation and stem cells theories. Therefore, in this study, we tried to evaluate the effects of resveratrol on cell migration and the expression level of VEGF, KRAS, and IDO1 -as cell progression-related factors- in MenSCs of endometriosis patients.
Materials and Methods: Healthy and endometriosis derived-MenSCs were purchased and cultured to reach 70% confluence. Endometriosis MenSCs were treated with 100 M of resveratrol (resveratrol group) for 3 days, while in positive (healthy) and negative (endometriosis) control groups, cells did not receive any treatment during 3 days of culture. To test the migration ability and gene expression level of cells, scratch test (assessed in time points of 12, 24, and 36 hours), and real-time polymerase chain reaction (PCR) were applied, respectively.
Results: The obtained results showed that at the time point of 36 hours, cells in resveratrol group had a statistically significant lower rate of wound closure than in endometriosis group (P= 0.047). Moreover, a significantly lower expression of *KRAS* and *VEGF* genes in Resveratrol group was observed comparing to the Endometriosis group (P=0.048 & P=0.02, respectively). However, treating with resveratrol could not decrease the IDO1 expression level of resveratrol group in compare to endometriosis cells (P=0.064).
Conclusion: According to the findings, resveratrol may ameliorate endometriosis progression through reducing the migratory ability of cells and decreasing the expression of VEGF and KRAS in endometriosis MenSCs.
Keywords: Endometriosis, Menstrual Blood-Derived Stem Cells, Migration Resveratrol

Ps-20: The Effect of miR-149-3p Encapsulated in Exosomes Isolated from Menstrual Blood-Derived Stem Cells in Inhibiting Proliferation and Cell Cycle (G1/S) of Breast Cancer

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Objective: Breast cancer is the most frequent cancer in women. Today, it is well acknowledged that common cancer treatments are inefficient and ineffective. Therefore, numerous investigations on new treatment alternatives with fewer side effects have yielded encouraging results. Stem cells are recognized as a possible source of cancer treatment and can be used as a tool in gene therapy. Stem cells secreted exosomes are the main agents in their therapeutic effects. In cancer treatment, exosomes can be utilized as carriers of medicines and functional RNAs. The purpose of this study was to explore the influence of mir-149-3p encapsulated in exosomes isolated from menstrual blood derived Stem cells (MenSCs) on the proliferation and cell cycle of the MDA-MB-231 cell line.
Materials and Methods: MenSCs were isolated and cultured until third passage. Then Cells were transfected with miR-149-3p, and the exosome isolation was done from both transfected and non-transfected MenSCs. The MDA-MB-231 cells was then treated with miR-containing exosomes (T-Exo)/ Exosome (Exo), and the subsequent changes in the mRNA and protein levels of AKT2 and ESR1 were investigated using real-time polymerase chain reaction (PCR) and western blotting, respectively. The amount of apoptosis was also assessed using AnnexinV/PI.
Results: Based on the data, AKT2 and ESR1 mRNA level were significantly decreased in T-Exo and Exo groups comparing to the control (P≤0.05). ESR1 protein level was also significantly lower in both treated groups than the control group, but T-Exo group showed significantly lower level comparing to the Exo group. Although, there were no significant change in the protein level of AKT2 among groups (P>0.05), in case of pAKT2, as the functional form of AKT2, lower protein level in T-Exo group was observed comparing to the control. Moreover, both T-Exo and Exo groups showed increased total apoptosis than the control group (P≤0.05).
Conclusion: It seems that both miR-149-3p and exosomes have the potential to be more studied and applied in novel cancer therapeutic approaches.
Keywords: Breast Cancer, Cell Proliferation, Cell Cycle, Exosome, MiR-149-3p

Ps-21: Evaluation of Biocompatibility and Osteoinductivity Properties of A Plant-Based Cellulose Scaffold: *In Vitro* and *In Vivo* Analysis

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Objective: Tissue engineering (TE) offers promise for treating bone defects in cases where self-healing is not possible. However, some TE-scaffolds lack sufficient biocompatibility essential for cell attachment, proliferation, tissue integration, and minimizing adverse reactions. Natural cellulose scaffolds show a great potential in addressing these challenges. *In vitro* analysis assesses the biocompatibility of cellulose scaffolds on human cells, but *in vitro* findings may not always directly translate to *in vivo* biocompatibility. Therefore, further preclinical testing is necessary to assess their safety and effectiveness for TE applications.

Materials and Methods: Towards the goal of developing a functional biocompatible system for bone TE, we assessed the cellular and tissue compatibility of a porous, fibrous scaffold derived from Monocephala leaves in both *in vitro* and *in vivo* settings. Osteoinductivity was evaluated by studying its effects on human mesenchymal stem cells (hMSCs) differentiation.
Results: Results showed biocompatibility in both models, supporting cell attachment, proliferation, mineralization, and infiltration. Histological analysis revealed a temporary foreign body response post-implantation, diminishing over time. The scaffold's properties, including biocompatibility, hydrophilicity, and mechanical strength, promoted new blood vessel formation, encouraging tissue regeneration.
Conclusion: Enhanced expression of bone markers in cultured cells suggested high potentials of these scaffolds to safe repair osteochondral defects without the risk of toxicity or an immunological reaction. These findings contribute to a better understanding of the cellulose scaffold's biocompatibility and osteoinductive properties, enhancing strategies for bone-TE development.
Keywords: Cellulose Scaffolds, Regenerative Medicine, Stem cell Differentiation, Tissue Engineering

Ps-22: Assessment of The Antibacterial and Wound Healing Effects of Magnesium Oxide Nanoparticles in Male Rats

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Objective: The severity and slow healing process of burn wounds make their treatment a significant challenge. This study aims to investigate the potential of magnesium oxide nanoparticles (MgONPs) in improving the healing process of skin wounds *in vivo*.
Materials and Methods: In the present study, a comprehensive assessment was conducted to investigate the antibacterial and cytotoxic activity of MgONPs. Male Wistar rats with deep burns were randomly assigned to different treatment groups, including untreated burns, silver sulfadiazine (1%), and MgONPs. The effects of these treatments on macroscopic and microscopic tissue alterations were evaluated over a period of 21 days.
Results: The study observed the antibacterial activity of MgONPs against gram-positive bacteria Staphylococcus aureus. The groups treated with MgONPs showed a significant increase in wound closure compared to the untreated group ($P<0.05$). However, the group treated with nanoparticles exhibited the highest rate of wound healing. The histologic results confirmed the healing activity of skin wound by MgONPs.
Conclusion: The use of a MgONPs has shown significant improvement in the microscopic appearance of burn wounds. These findings suggest that the inclusion of nanoparticles in the ointment may expedite the healing process.
Keywords: Burn, Magnesium Oxide, Nanoparticles, Skin

Ps-23: Evaluation of Anticancer Effects of Linoleic Acid-Loaded Niosomes on Hepatocellular Carcinoma Cells

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Objective: Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, which is the second leading cause of cancer deaths in the world. Due to the ineffectiveness of common treatments, there is a serious need to find more effective and targeted treatments. Niosomes are one of the common types of nanoparticles in modern drug delivery systems, which are receiving attention nowadays. The purpose of this study was to synthesis, characterize the physicochemical properties of niosomes containing linoleic acid (LA) (an essential fatty acid with anticancer effects) and evaluate their effects on HCC cells (Hep 3-B).
Materials and Methods: We synthesized LA-loaded niosomes by thin film hydration method and characterized their size, polydispersity index (PDI) and zeta potential by zeta sizer (DLS (and morphology of niosomes was evaluated by scanning electron microscope (SEM). Also, we evaluated the toxicity effects by MTS assay and migration capacity of treated cells with 150 μM of LA-loaded niosomes, free niosomes, free LA and control group (non-treated cells) by scratch assay.
Results: Niosomes had size of 105.7 nm, PDI of 0.271 and -26.1 mV zeta potential. The SEM results indicated that niosomes had appropriate morphology. Niosomes with entrapment efficacy (EE) 74%, released LA slowly and sustained. The MTS assay results indicated that LA-loaded niosomes were more toxic than free LA to Hep-3-B cells. But they showed no toxic effects on normal cells (HFF). Also, LA-loaded niosomes reduced migration capacity of Hep-3-B cells better than other groups.
Conclusion: The use of niosome as a nanocarrier can be a good way to target and destroy cancer cells since they have toxic effects on HCC cells and could reduce migration rate of them.
Keywords: Hepatocellular Carcinoma, Niosome, Linoleic Acid

Ps-24: Optimizing Cryopreservation of HESC-Derived RPE Cells to Comply with GMP Conditions

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Objective: Cryopreservation is a critical step for Advanced Therapy Medicinal Products (ATMPs) that adhere to Good Manufacturing Practice (GMP) regulations to achieve the highest possible cell recovery rate while preserving the properties and function of the cells. However, a point to consider when manufacturing a drug product under GMP conditions is the use of reagents to simplify clinical delivery. We previously used a combination of compounds to freeze human embryonic stem cells-derived retinal pigment epithelial (hESC-RPE) cells consisting of 10% DMSO, 40% RPE medium, and 50% knockout

serum replacement (KOSR). In this study, we intend to develop a new freezing formulation for hESC-RPE cells that complies with GMP regulations.
Materials and Methods: We tested the use of two concentrations of DMSO (5 and 10%) and replaced KOSR and RPE medium with human serum albumin (HSA) at concentration of 5 and 10%, and BSS PLUS, respectively, in previous freezing media for cryopreservation of hESC-RPE cells. After 1 week, 1, 3 and 6 months, we thawed the hESC-RPE cells and assessed their survival, morphology, attachment, and RPE markers to compare with the frozen cells in the previous group (control group).
Results: The results showed no significant difference between the GMP formulation media and the control group in cell viability and cell attachment. Furthermore, RPE cells showed pigmented and cobblestone morphology 10-15 days after thawing and expressed CRALBP and MITF markers in all groups.
Conclusion: Our research suggests that low concentrations of DMSO in combination with HSA and BSS PLUS are suitable excipients for freezing hESC-RPE cells for therapeutic purposes.
Keywords: Cryopreservation, GMP Conditions, Retinal Pigment Epithelial Cells

Ps-25: Investigating The Effect of Toll-Like Receptor 4 Inhibition on The Osteogenic Differentiation of Mesenchymal Stem Cells Under Inflammatory Conditions

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Objective: Rheumatoid arthritis (RA) is an autoimmune disease that affects the synovial lining, leading to joint damage and the destruction of cartilage and bone tissue. Research has shown that blocking the activation of Toll-like receptor 4 (TLR4) pathway, can prevent the progression of inflammatory diseases like RA. TAK-242 is a small molecule that specifically inhibits the TLR4 pathway. On the other hand, according to studies, the TLR4 pathway plays a role in osteogenesis. The present study investigated how inhibiting the TLR4 pathway affects the osteogenic differentiation of bone marrow mesenchymal stem cells (BM-MSCs) under inflammatory conditions.
Materials and Methods: BM-MSCs were isolated from rats, cultured, and characterized to confirm their properties. The toxicity of TAK-242 was evaluated using MTS assay. To induce inflammatory conditions, BM-MSCs were treated with 1 µg/ml of LPS. The expression of inflammatory genes and cytokines in BM-MSCs was done by real-time polymerase chain reaction (PCR) and ELISA methods after 24 or 48 hours. Evaluations were done between the control, LPS, and LPS+TAK-242 groups. Finally, real-time PCR and Alizarin red staining were performed to evaluate the effect of TAK-242 on osteogenic differentiation of BM-MSCs on day 7.
Results: The MTS assay indicated that 100 nM is the optimal dose of TAK-242. Real-time PCR and ELISA results demonstrated that TAK-242 decreased the expression of inflammatory genes TNFα and IL-6 in BM-MSCs compared to the control group. Alizarin red staining and osteogenic genes expression showed that TAK-242 did not inhibit the osteogenic differentiation of BM-MSCs under inflammatory conditions.
Conclusion: TAK-242, by inhibiting the TLR4 pathway, not only inhibits inflammation but also can play a role in bone repair. As a result, TAK-242 can be used as a therapeutic approach for RA disease. However, further studies are required for verification.
Keywords: Mesenchymal Stem Cells, Osteogenic Differentiation, Rheumatoid Arthritis, Toll-Like Receptor 4, TAK-242

Ps-27: Therapeutic Potential of Hair Follicular Stem Cells Conditioned Medium in Vascular Dementia: Insights into Cellular and Molecular Mechanisms

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Objective: Vascular dementia (VaD) represents a prevalent form of dementia with significant clinical implications. This study aimed to delve into the cellular and molecular mechanisms underlying the effects of hair follicular stem cells conditioned medium (HFS-CM) in VaD.
Materials and Methods: Forty-eight rats were divided into four groups: control, sham operation, VaD + vehicle, and VaD + HFS-CM. CM was administered intraperitoneally on days 4, 14, and 24 post-2VO induction. Cognitive performance was assessed using open-field (OP), passive-avoidance, and Morris-water maze tests. Field-potential recording evaluated basal synaptic transmission (BST) and long-term potentiation (LTP). Hippocampal tissue was dissected for real-time polymerase chain reaction (PCR) analysis of *β1-catenin*, *IGF-1*, *TGF-β*, *GSK-3β*, *PSD-95*, and *NR2B* gene expression.
Results: VaD rats exhibited impaired performance in behavioral tests, along with reduced BST and LTP induction. Gene expression analysis revealed decreased levels of *β1-catenin*, *IGF-1*, *PSD-95*, and *TGF-β*, alongside increased *NR2B* and *GSK-3β* expression. HFS-CM treatment restored *PSD-95* and *GSK-3β* expression, improved fear memory and spatial learning, and enhanced grooming behavior. However, memory retrieval and exploratory behavior remained unaffected. While BST recovered with HFS-CM administration, LTP induction remained impaired.
Conclusion: This study highlights the therapeutic potential of HFS-CM in VaD, primarily through its role in restoring BST and improving gene expression profiles, ultimately leading to the amelioration of fear memory deficits.
Keywords: Conditioned Medium, Long-term Potentiation, Memory, Synaptic Transmission, Vascular Dementia

Ps-28: A Three-Dimensional Alginate and Alginate Methyl Cellulose Lung Cancer Culture: Characterized Model for Infection and Drug Testing Study

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Objective: In last decade, researchers have been tried to develop different three-dimensional (3D) cell cultures system, these systems are valuable due to potential of mimicking *in vivo* structure and cell-cell communication along with different applications such as drug discovery, tissue engineering, compound screening, vaccine test and personalized medicine to model different diseases. Limitation in access to proper model during pandemic showed requirement of effective and feasible model as immense help to researcher.
Materials and Methods: Therefore, we developed a 3D culture setting of A549 lung cancer cells (human alveolar basal epithelial cells) using alginate beads and alginate MC tested its effectiveness in different conditions. The viability and proliferation of cells were assessed using Alamar blue, the size and morphology was checked by ImajeJ, SEM microscopy and Immunofluorescent assessment in different days (0, 3, 5, 7, 10 in compare with scaffold alone and 2D culture).
Results: Cell viability for A549 resulted in considerable increase in day 5 for Alg group in compare with Alg-MC. in addition, in both group day 5 showed highest size but Alg group had a higher diameter than Alg-MC. SEM result also indicated increased porosity for Alg rather than Alg-MC. Characterization of spheroids by Immunofluorescence showed distinct assembly of Factin filament around the aggregated cells.
Conclusion: In summary, both biomaterials are appropriate to get accurate 3D model suitable for drug testing and viral infection.
Keywords: Alginate, Diseases Modeling, Lung Cancer, Methyl Cellulose, 3D Culture

Ps-29: Do Inhibitors of Apoptosis Proteins Play Role during Differentiation of Human Embryonic Stem Cells into Cardiomyocytes?

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Objective: Caspases are known for their critical roles in inflammation and apoptosis. Increasing evidence, however, has revealed diverse functions for caspases such as promoting differentiation and development of variety of cell types. In the case of differentiation into cardiomyocytes, the non-apoptotic function of caspases, activated through mitochondrial pathway, has been well-documented, indicating a highly precise regulatory mechanism. Inhibitors of apoptosis proteins (IAPs) are the most popular caspases inhibitors which have been less studied in differentiation.
Materials and Methods: To explore whether IAPs, control caspases activity at non-lethal level, the smac-mimetic Brinapant was used in order to antagonize multiple IAPs including XIAP, cIAP-1, and -2 during cardiomyocyte differentiation from human embryonic stem cells (hESCs). Real-time RT-qPCR and western blotting were performed to analyze IAPs expression level. The activation pattern of caspase-9 and -3 was also investigated by western blotting and caspase-like activity assay in differentiating and apoptotic cells.
Results: Brinapant-treated hESCs were differentiated into beating cardiomyocytes with an efficiency comparable to that of untreated cells. This suggested that IAPs may not be the main regulators of caspases during differentiation or expressed at an insufficient level in our study. On the other hand, the results showed functional cleaved caspase-9 in hESCs with a reducing trend at early stages of differentiation, without activation cleavage of cellular caspase-3.
Conclusion: Taken together, our findings suggested that caspase-9-cleavage of caspase-3 may be inhibited by factors besides IAPs, ensuring protection of pluripotent and differentiating cells from apoptosis in the presence of active caspase-9. Further study is expected to clarify the caspase regulators during cardiac differentiation, elucidating the molecular mechanisms involved, with diagnostic and therapeutic approaches.
Keywords: Caspases, Cardiogenesis, Cell Differentiation, Human Embryonic Stem Cells (hESCs), Inhibitors of Apoptosis Proteins (IAPs)

Ps-30: Nicotine Exposure Alters Expression of Stemness-Related Genes in Human Colorectal Cancer Cell Line

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Objective: Epidemiological studies have suggested that cigaret smoking is associated with increased colorectal cancer (CRC) risk. Nicotine is most likely related to the risk of cigaret smoking and exerts many of its effects on cancer cells through the α7-subtype of nAChR (α7nAChR). The development of CRC originated from cancer stem cells, which comprise a minor population of CRC cells. However, the mechanisms by which nicotine influences the stemness properties of cancer cells are not fully understood.
Materials and Methods: To examine the influence of nicotine exposure on cancer stem cell-related gene expression, the present study applied real-time RT-PCR to investigate changes in cancer stem cell-related gene expression in SW-480 CRC cells exposed to nicotine. SW-480 cells were inoculated in 6-well plates to determine the effects of treatments with 1 μM and 10 μM concentrations of nicotine on the expression level of α7nAChR and cancer stem cell markers, including Nanog, Oct-4, Sox-2, CD 44, CD 133, and aldehyde dehydrogenase (ALDH), by quantitative real-time polymerase chain reaction (PCR).
Results: The findings showed that nicotine increases the expression of both α7nAChR and cancer stem cell marker mRNA expression. Transfection with α7nAChR-siRNA prevented the observed effects of nicotine, indicating that these effects of nicotine are α7nAChR dependent.
Conclusion: Nicotine has recently been found to enhance the stemness properties of cancer cells. Nicotine alters Nanog, Oct-4, Sox-2, CD 44, CD 133, and ALDH expression in the SW-480 cell line and exerts its effects through the α7nAChR dependent axis. Studying the exact molecular mechanism of nicotine signaling can be useful both in diagnosing and treating nicotine-

related cancers and in identifying novel potential therapeutic benefits.
Keywords: Cancer, Nicotine, Nicotinic Receptors, Stemness, SW-480

Ps-31: Investigating The Role of Thermosensitive Hydrogel for The Sustained Delivery of Exosomes Extracted from Menstrual Blood Mesenchymal Stem Cells on Triple-Negative Breast Cancer Cells

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Objective: Due to the heterogeneity of triple-negative breast cancer (TNBC), conventional treatments respond poorly, and there is no targeted treatment for this cancer. Menstrual blood stem cell exosomes (Exo-Mens) have been shown to be potent inhibitors of tumor-induced angiogenesis in prostate and breast cancer models. This study was conducted with the aim of investigating the effects of hydrogel-containing Exo-Mens on breast cancer cells.
Materials and Methods: Optimization and characterization of the hydrogel was conducted, then MDA-MB-231 and human umbilical vein endothelial cells (HUVEC) were examined in two groups of hydrogels (control) and hydrogel with Exo-Mens. Initially, the IC_{50} of Exo-Mens was determined by the MTT assay, and the degradability and release pattern of the studied groups were measured. Western blot (VEGF, HIF-1α) and qRT-polymerase chain reaction (PCR) (VEGF, HIF-1α, and KDR) were performed for the HUVEC cell line, and scratch tests, colony formation, apoptosis, and migration for the MDA-MB-231 cell line, and invasion were performed for both cell lines.
Results: The angiogenic activity of Exo-Mens within the hydrogel, revealed a significant shift in the expression of pro-angiogenic genes and related proteins including HIF-1α, VEGFA, and KDR, in the treated HUVECs. The treatment group of hydrogel was also able to reduce migration and invasion in both cell lines compared with the control group. In addition, reduction of colony formation and an increase in apoptosis were observed, especially in cancer cells.
Conclusion: The developed hydrogel system containing Exo-Mens was able to prevent both the proliferation and invasion of tumor cells as well as the formation of angiogenic cells.
Keywords: Anti-Angiogenesis, Exosome, Hydrogel, Menstrual Stem Cells, TNBC

Ps-32: The KDM6A Upregulation Reduced The Cancerous Phenotype in The Gastric Adenocarcinoma Cell Line

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Objective: Gastric cancer is a significant global health concern. About 90% of gastric cancer cases are gastric adenocarcinoma, which ranks fifth in the world in terms of the prevalence of the disease and the third most common cause of death. One of the most common changes in the development of cancer is epigenetic changes. Methylation and demethylation of histones are among these changes. KDM6A is one histone demethylase that mutates in gastric cancer and is role-critical in the process of carcinogenesis. This gene has demethylase activity and removes the trimethyl group from histone 3 lysine 27 and causes transcription and expression. In this study, we will examine the effect of KDM6A overexpressing on the induction of apoptosis rate and reduction of proliferation, viability, and migration of AGS cells so that this molecule can be used as a therapeutic target in the field of molecular targeted therapies.
Materials and Methods: A Lentiviral vector was used to induce KDM6A force expression in AGS cells. Then, the effect of KDM6A force expression on the cancerous phenotype of cells was assessed by assessing their apoptosis, wound healing, colony formation assay, MTS assay, and gene expression in transduced AGS cells.
Results: Force expression of KDM6A induces apoptosis rate and decreases the viability, migration rate, colony formation capacity, and altered specific gene expression in the transduced AGS cell compared to the control group.
Conclusion: Force expression of KDM6A reduces cancerous phenotype which has significant advantages for the diagnosis and treatment of patients and could be hoped for targeted therapy for gastric adenocarcinoma treatment.
Keywords: Cancerous Phenotype, Gastric Adenocarcinoma, KDM6A, Lentivirus Vector, Molecular Targeted Therapy

Ps-33: KDM6A Over-Expression Attenuated Epithelial-Mesenchymal Transition and Induced Mesenchymal-Epithelial Transition in Hepatocellular Carcinoma Cells

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Objective: About 90% of liver cancer is hepatocellular carcinoma and fourth most common cancer and the third leading cause of cancer-related death in the world. Despite the common treatments after surgery, due to the remaining microscopic metastasis residues, the possibility of cancer recurrence is high. Therefore,

molecular-targeted treatments are very important. During the initiation of liver cancer, the progression of epithelial to mesenchyme transition (EMT) is observed. These changes result in increased invasion and metastasis capacity of cancer cells. In liver malignancies, one of the mutations that in the histone modification happens is the down-regulation of KDM6A. KDM6A is a histone demethylase and a key molecule in regulating cell proliferation, development, and division. Mutations of KDM6A are indicated in cancer types. This research investigates the changes in the EMT-MET (Mesenchyme to epithelial transition) process of hepatocytes after up-regulation of the KDM6A in the hepatocellular carcinoma cells

Materials and Methods: A Lentiviral vector was used to induce KDM6A overexpression in Huh-7 human hepatic cells. We evaluated the effect of KDM6A overexpression on the EMT-MET process, migration rate, wound healing, and change morphology.

Results: KDM6A upregulation reduced the migration rate, in transduced Huh-7 cells. Moreover, the expression pattern of EMT-MET process-related markers in HCC cells was changed.

Conclusion: Our study indicated that the up-regulation of KDM6A could be used as a potential non-invasive therapeutic strategy for preventing cancer metastasis and recurrence inhibition and inducing the MET process in HCC cells. It is expected that this research proposes a molecular therapeutic target, and opens innovative ways to create suitable treatments for hepatocellular carcinoma.

Keywords: Epithelial-Mesenchymal Transition, Hepatocellular Carcinoma, KDM6A, Mesenchyme to Epithelial Transition, Migration Rate

Ps-34: Innovative Liver Cell-Based Platforms; A New Insight in Drug Screening and Toxicology

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Objective: Hepatocytes plays a crucial role in drug screening due to their essential liver functions and detoxification capabilities. Current research focuses on hepatocyte toxicity, using hepatocytes sourced from normal livers, stem cell-derived hepatocytes, and various cancer cell lines. Challenges in working with these cells include limited accessibility, rapid dedifferentiation and loss function. Previous studies have explored pathways related to liver development and liver cancer, identifying key genes such as *HNF4α* a crucial transcription factor in hepatogenesis. Also, *HNF4α* is vital for preserving the phenotype and normal function of hepatocytes. Multiple studies have reported a reduction in the expression of *HNF4α* in liver cancer.

Materials and Methods: In this study a novel approach was employed to increase the expression of the key gene *HNF4α* in Huh7 cancer cells using SINEUP technology in a 3D culture. Manipulated Huh-7 were co-culture with HUVEC and MSC cells, and microparticle-derived sheep liver ECM for mimicking realistic micro environment. The micro-tissue comprised of upregulated HNF4α-Huh7 cells was designated as the experimental group, while the micro-tissue consisting of Huh-7 cells served as the control group. Comparative analyses were implemented on morphological characteristics, mRNA and protein expression, and functional test between the control and experimental microtissue groups.

Results: Significant differences were observed in the expression of metabolic genes at the mRNA, protein levels, and functional characteristics following the upregulation of the *HNF4α* gene in experimental microtissues compare to control microtissues.

Conclusion: By upregulating the expression of the *HNF4α* in Huh7 cells, this study demonstrated that the characterization and function of these cells become more similar to normal hepatocytes. The findings suggest the potential of developing 3D platforms based on engineered cancerous cells to address challenges in drug screening and toxicology in a more cost-effective manner.

Keywords: Drug Screening, Hepatocyte, HNF4α, Innovative Cell-Based Platforms

Ps-35: Tapping into The Potential of Cancer Stem Cell Gene Editing For Gene Therapy

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Objective: Glioblastoma is an aggressive brain cancer with a poor prognosis, and cancer stem cells (CSCs) are believed to play a crucial role in its development and treatment resistance. Recent advances in gene editing technologies, particularly CRISPR/Cas9, have created novel opportunities for targeting cancer stem cells in glioblastoma. The utilization of CRISPR/Cas9 has been observed in targeting crucial signaling pathways and genes responsible for maintaining glioblastoma cancer stem cells. Studies have shown that targeting the Hedgehog pathway, crucial for cancer stem cell self-renewal, can effectively inhibit their proliferation and improve treatment outcomes. Additionally, CRISPR/Cas9 has been employed to disrupt the expression of genes associated with cancer stem cell stemness, such as SOX2, Nanog, and Oct4. Downregulation of these genes has been shown to reduce the tumorigenic potential of glioblastoma cancer stem cells and sensitize them to conventional therapies. Researchers have also used CRISPR/Cas9 to target epigenetic regulators that maintain the cancer stem cell state, such as the histone demethylase JMJD3. Inhibition of JMJD3 has been proven to impair the self-renewal and differentiation capabilities of glioblastoma cancer stem cells.

Materials and Methods: In our research, we conducted a comprehensive review of data and research in this field, utilizing bioinformatics resources and in silico work, to inform our study. This approach enabled us to gather an extensive understanding of the subject and build a strong foundation for our research.

Results: Based on the GSE107560 dataset, miR-21 appears to be the most promising target for glioblastoma stem cell gene editing for GBM gene therapy. miR-21 was identified as one of the most significantly deregulated miRNAs in glioblastoma stem cells compared to differentiated tumor cells. Targeting miR-21 has been demonstrated to inhibit glioblastoma growth, and the TCGA data analysis also associated high miR-21 expression with poorer patient survival outcomes.

Conclusion: Overall, the utilization of CRISPR/Cas9 in glioblastoma cancer stem cell research offers valuable insights into the molecular mechanisms underlying cancer stem cell maintenance and has exposed new avenues for targeted therapies. As this field continues to evolve, the integration of CRISPR/Cas9-based strategies with other emerging technologies will further enrich our comprehension of glioblastoma cancer stem cells and lead to more effective treatment strategies.
Keywords: Cancer Stem Cell, CRISPR/Cas9, Gene Editing, Glioblastoma, Targeted Therapies

Ps-36: Effects of Conditioned Medium of Human Adipose-Derived Mesenchymal Stem Cells on Apoptosis of Endometriosis Cells

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Objective: Although the pathogentic mechanisms related with endometriosis are not clearly understood, apoptosis seems to play a critical role . This research is to detect if Conditioned Medium (CM) obtained from human adipose tissue-derived mesenchymal stem (AD-MSCs) can promote apoptosis in Menstrual blood-derived stem cells (MenSCs) in women with endometriosis.
Materials and Methods: About 2 mL of menstrual blood collected from infertile women. MenSCs were cultured up to passage 3 and cell surface markers were analyzed by flow cytometry. To study the effect of CM on apoptosis of endometriosis cells, Annexin V assay followed by flow cytometry analysis was used.To further analyze the effect of CM on apoptosis and survival of endometriosis cells, mRNA expression of *BAX*, *Bcl-2* and survivin was studied using real-time polymerase chain reaction (PCR).
Results: Apoptosis analysis by flow cytometry showed that late apoptosis and early apoptosis significantly increased in comparision with control group.The real-time PCR findings demonstrated that mRNA expression of *BAX* significantly increased as compared with untreated. in this study no significant differences were detected in mRNA expression of *Bcl-2* and *Survivin* between the groups.
C**onclusion:** The research demonstrate that CM could enhance apoptosis in endometriosis. Furthermore, the findings indicate that MenSCs may have a pivotal role in the pathogenesis of endometriosis and further validate the theory of endometriosis formation through retrograde menstrual blood flow.
Keywords: Apoptosis, Conditioned Medium, Endometriosis, Mesenchymal Stem Cells (MSCs), Menstrual Blood

Ps-37: The Effect of Conditioned Medium Obtained from Human Adipose-Derived Mesenchymal Stem Cells on The Restoration of Spermatogenetic Genes in A Rat Model of Azoospermia Induced by Busulfan

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Objective: For men with non-obstructive azoospermia (NOA), assisted reproductive techniques (ART) are often the only viable option to have a biological child. This study aims to investigate whether Conditioned Medium (CM) from Human adipose tissue-derived mesenchymal stem cells (AD-MSCs) can help to restore the expression of spermatogenic genes in a busulfan-induced azoospermic rat model.
Materials and Methods: To investigate the impact of CM intratestis injection on spermatogenesis recovery in a rat model of NOA , AD-MSCs were isolated and cultured. The CM was collected on the 3rd passage. The rats (30 male Wistar rats, aged 8-12 weeks) were divided into 4 groups: control group (no treatment), NOA group (busulfan-induced rats), azoospermia sham group (busulfan + Phosphate-buffered saline), and experimental group (busulfan + ADSC-CM). The NOA model was induced by intraperitoneal busulfan injections with a 21-day interval. After 35 days, the test group received ADSC-CM. Gene expression was analyzed using real-time polymerase chain reaction (PCR).
Results: The analysis indicated a significant increase($P \leq 0.5$) in the levels of DAZL, Miwi and VASA expression within the ADSC-CM group as compared to the control group, whereas a significant decrease was observed in the NOA and Sham groups.
Conclusion: This study suggests that the use of CM obtained from AD-MSCs could potentially assist in the recovery of spermatogenesis in busulfan-induced infertile rats.
Keywords: Adipose Mesenchymal Stem Cells, Conditioned Medium, Non-Obstructive Azoospermia

Ps-38: Human Three-Dimensional Acellular Amniotic Membrane Containing Adipose Tissue-Derived Mesenchymal Stem Cells; How Deep Is The Penetration of Allogenic Stem Cells into The Scaffold?

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Objective: Simulation of *in vivo* conditions for mesenchymal stem cells in a laboratory environment and placing them on a biological ECM can not only improve the structural characteristics of stem cells but also significantly increase their secretory potential and function.
Materials and Methods: In this study, mesenchymal stem cells were extracted from adipose tissue, cultured until passage 3, and confirmed by flow cytometry and differentiation potential. In the next step, the amniotic membrane separated from placenta was decellularized using mechanical and chemical methods. According to the convergent scattering pattern, activated allogeneic mesenchymal stem cells (7×10^5 cells/each scaffold) were propagated for 16±3 hours at 37°C, 5% CO_2 and 90% humidity. The structural, mechanical, biological, and physicochemical health of 3D scaffold was confirmed using SEM, MTT, FTIR and acridine orange staining methods. Safety and efficiency of 3D scaffolds were investigated in the healing process of diabetic wounds in C57 mice.
Results: We designed a three-dimensional biological scaffold composed of decellularized amniotic membrane with a diameter of 20-25 µm, which contains active allogeneic mesenchymal stem cells derived from adipose tissue with a diameter of 1.8-2.8 µm. Allogeneic mesenchymal stem cells not only settled and proliferated on the surface layer of acellular amniotic membrane but also permeated into deeper layers and formed a multilayered

structure. SEM analysis demonstrated that the allogeneic mesenchymal stem cells penetrated into the acellular amniotic membrane from a depth of 5µm to 17µm. The structural, mechanical, biological, and physicochemical health of scaffolds was confirmed using SEM, FTIR, MTT, and acridine orange staining methods. There were no allergic and immunological reactions in treated diabetic mice after treatment.
Conclusion: The 3D amniotic membrane scaffold can have wide therapeutic applications, not only in plastic surgery, tissue engineering, and regenerative medicine, but also in treatment of gynecological and reproductive system diseases, cardiovascular abnormalities, etc.
Keywords: Amniotic Membrane, Mesenchymal Stem Cells, 3D Biological Scaffold

Ps-39: Effects of Kartogenin-Enriched MSC Extracellular Vesicles with Hyaluronic Acid on Chondrogenesis of MSCs Derived from Arthritic Rats

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Objective: Rheumatoid Arthritis (RA), is an autoimmune disease that damages the synovial membrane, cartilage, and bone. Despite advances in cell therapy, RA treatment still faces significant challenges. However, extracellular vesicles (EVs) derived from MSCs show promise as future clinical alternatives. These EVs serve as nanocarriers for miRNAs, and small molecules including kartogenin (KGN), which notably promotes chondrogenesis. The primary challenge lies in targeted drug delivery. This study aims to enhance EV-KGN by applying a hyaluronic acid (HA) coating, potentially leading to more effective drug delivery and improved chondrogenesis *in vitro*.
Materials and Methods: Bone marrow-derived mesenchymal stem cells (Bm-MSCs) were isolated from an arthritis rat model. These cells were differentiated into osteogenic, adipogenic, and chondrogenic lineages. Extracellular vesicles (EVs) from BM-MSCs, obtained through ultracentrifugation, were characterized. KGN (kartogenin) was encapsulated into EVs, and a modified hyaluronic acid (HA) coating was applied. The study evaluated the chondrogenic potential of experimental groups, including EV, KGN, EV-KGN, chondrogenic media, and HA-EV-KGN, using toluidine blue staining and qPCR to measure gene expression related to chondrogenesis.
Results: The identity of Bm-MSCs was confirmed based on their spindle-shaped morphology and differentiation into skeletal lineages. EV-MSCs were characterized by their size (70 to 150 nm) and the presence of the EV marker CD63. Histological results showed cartilage cell matrix formation in all experimental groups. As qPCR, all experimental groups had significantly higher expression of chondrogenic genes (COL II, SOX9, and COL X) compared to control MSCs. Notably, the HA-EV-KGN group exhibited significantly higher expression of these genes compared to other experimental groups (**P<0.01).
Conclusion: The HA-EV-KGN group showed significantly increased delivery of hyaluronic acid (HA)-enriched extracellular vesicles (EVs) targeting chondrogenesis compared to other groups. Importantly, using HA-EVs led to reduced drug consumption. Overall, HA-EV-KGN holds promise as an effective system for targeted drug delivery and therapeutic applications.
Keywords: Extracellular Vesicles, Chondrogenesis, Hyaluronic Acid, Mesenchymal Stem Cells, Kartogenin

Ps-40: Reversing Hepatic Stellate Cell Activation to Attenuate Liver Fibrogenesis by Placenta Derived Biomaterials

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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 stimulated with TGFb for 24 hours and then treated with placental biomaterials for 24 hours. Cell proliferation was determined by BrdU assay. Intracellular ROS levels were evaluated using 2',7'-dichlorofluorescin diacetate (DCFH-DA) staining and mRNA expression of oxidative stress related genes was shown. Protein expression and mRNA expression of ECM components were evaluated. Cell migration was evaluated using trans-well assay and mRNA expression of EMT-related genes was determined.
Results: Placental biomaterials attenuate hepatic stellate cell activation through regulating the cell proliferation, 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: Biomaterials, Hepatic Stellate Cell, Liver Fibrosis, Regenerative Medicine

Ps-41: Designing of Single Guide RNA for Melanogenesis Assay in Zebrafish

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Objective: Many human diseases are deeply intertwined with genetics, underscoring the critical importance of understanding this relationship in the context of therapeutic interventions. Among the array of genetic manipulation technologies, CRISPR-Cas9 stands out for its unparalleled precision in gene editing. Widely embraced for its ability to generate animal and cell models, CRISPR-Cas9 holds significant promise for advancing

genetic studies. Zebrafish, with their transparent embryos and rapid developmental pace, emerge as particularly valuable models for exploring the genetic underpinnings of human diseases. Notably, the *SLC24A5* gene is recognized as a key player in melanogenesis, with mutations often associated with various forms of albinism. In this study, our aim is to design and clone a single guide RNA (sgRNA) targeting the *Slc24a5* gene in zebrafish.
Materials and Methods: Our methodology hinges on precise molecular biology techniques. Initially, we retrieve the *Slc24a5* gene sequence from public databases, such as NCBI, followed by rigorous bioinformatic analysis to design sgRNAs using specialized tools like CHOP CHOP. The designed sgRNA constructs are then seamlessly integrated into the DR274 vector through enzymatic digestion and ligation using T4 enzyme at 37°C. The resulting constructs are introduced into competent E. coli cells for amplification, followed by cultivation in LB Broth medium and long-term preservation at -70°C.
Results: Validation of sgRNA integration into the vector was achieved through a series of meticulous experimental procedures, including colony polymerase chain reaction (PCR) and digestion assays. Furthermore, Sanger sequencing served as a robust quality control measure, ensuring the fidelity of the genetic constructs and guarding against unintended mutations. Three colonies were selected following successful confirmation procedures.
Conclusion: In the DR274 plasmid, sgRNA oligos are cloned under the control of the SP6 promoter, facilitating *in vitro* transcription of sgRNA. The resulting product holds potential for the knockout of the *Slc24a5* gene in zebrafish, thus offering a valuable model for studies related to albinism.
Keywords: CRISPR, Zebrafish, Genetic Manipulation, Melanogenesis

Ps-42: Three-Dimensional NanoFibers Play The Key Role in Regeneration of Neural Stem Cells

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Objective: To begin, spinal diseases, particularly spinal cord injuries (SCI), are severe conditions with no current cure, leading to significant burdens on patients due to permanent neurological impairments. Stem cell-based therapies, specifically neural stem cells (NSCs), have emerged as promising options for repairing injured spinal cords. Neural stem cells are multipotent stem cells capable of differentiating into neuronal and neuroglial cells, making them ideal candidates for regenerating damaged spinal cords. Controlling the fate of neural stem cells is crucial for effective spinal cord regeneration. Neural stem cells possess therapeutic potentials such as modulating inflammatory environments, supporting axonal growth, and differentiating into neural cells, all essential for spinal cord injuries repair. Nanofibers play a pivotal role in regulating the fate of stem cells for spinal cord regeneration. Electrospun fibers, with their ability to provide physical guidance cues and support axonal regeneration, have shown promise in neural tissue engineering applications, including spinal cord injury research. The latest innovation in this field involves three-dimensional nanofibers, which offer a solution to the limitations of conventional three-dimensional scaffolds by providing precise structures that match the spinal cord's architecture. These three-dimensional nanofibers can stimulate and guide axon regeneration, promoting functional recovery in spinal cord injuries.
Materials and Methods: In the course of our investigation, we undertook a thorough examination of data and studies within this particular domain. This methodology facilitated the acquisition of a profound comprehension of the topic and the establishment of a robust basis for our investigation, thereby guaranteeing that our discoveries are well-supported and rooted in current scientific understanding.
Results: By combining neural stem cells with three-dimensional biomimetic scaffolds, a significant advancements in promoting axonal regeneration and functional recovery in spinal cord injuries have been achieved, showcasing the potential of nanofibers in enhancing stem cell-based therapies for spinal cord regeneration.
Conclusion: In conclusion, the use of nanofibers, especially three-dimensional nanofibers, represents a cutting-edge approach in the field of spinal cord regeneration, offering new insights and possibilities for controlling the fate of neural stem cells and ultimately improving outcomes for patients with spinal cord injuries.
Keywords: Nanofiber, Neural Stem Cells, Regenerative

Ps-43: Anti-Inflammatory Effects of TAK-242-Enriched MSC Extracellular Vesicles with Hyaluronic Acid on Mesenchymal Stem Cells Derived from Arthritic Rats

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Objective: Rheumatoid arthritis (RA) is a chronic autoimmune disease that leads to bone and cartilage destruction. Inhibiting toll-like receptor (TLR) activity can halt inflammation. TAK242, a TLR4 inhibitor, has been used in RA and sepsis. On the other hand, MSCs- extracellular vesicles (EVs) are effective drug carriers. Recently, the surface modification of EV with hyaluronic acid (HA) is a promising targeted drug delivery method. This study investigates the effect of HA-modified EV-TAK242 on inflammation reduction.
Materials and Methods: MSCs were isolated from arthritic rat bone marrow and differentiated into osteogenic and adipogenic lineages. Optimal TAK-242 dosage was determined via the MTS test. EV-MSCs were obtained from the Royan Institute's ATMP center and characterized using DLS, western blot, and scanning electron microscopy (SEM). TAK-242 was introduced into EVs through electroporation. The EV surfaces were modified with hyaluronic acid. Inflammation amplified into rMSCs using LPS. After 48 hours, the anti- inflammatory effects of EV, TAK-242, EV-TAK242, and HA-EV-TAK-242 were examined on rMSCs. Subsequently, the expression of cytokines TGF-ß, IL-10, TNF-α, IL-6, and NK-KB were evaluated through qPCR, ELISA, and immunocytochemistry (ICC) techniques.
Results: Spindle-shaped morphology and rMSC differentiation into skeletal lineages confirm their mesenchymal characteristics. The identity of EVs was validated through the presence of

the CD63 marker and an EV size range of 70-150 nm. Post-treatment, the expression of anti-inflammatory genes TGF-β and IL-10 significantly increased across all groups compared to the control after 48 hours (**P<0.01). However, there was no significant difference in the expression of these genes between the TAK242 and EV groups (**P<0.001, *P<0.01). The ICC analysis showed the NF-κB expression decreased in rMSCs after 48 hours. ELISA assessment showed TNFα and IL-6 cytokines were decreased in all groups in comparison to the control group, while it was not statistically significant.
Conclusion: This study shows that HA-EV-TAK242 can reduce inflammation via labeling drugs for targeted release.
Keywords: Anti- Inflammatory Properties, Extracellular Vesicles, Hyaluronic Acid, Mesenchymal Stem Cells, TAK-242

Ps-44: Histopathological Evaluations of The Colon in Induced Ulcerative Colitis: The Role of The Supernatant of Mesenchymal Stem Cells Containing 17-Beta Estradiol

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Objective: The role of estrogen in the accelerating regeneration of the intestinal mucosa and the presence of estrogen receptors on the surface of mesenchymal stem cells (stimulator of proliferation and differentiation of MSC) led us to investigate the role of the supernatant of mesenchymal stem cells containing 17-beta estradiol in the histopathological changes of the colon of rats suffering from ulcerative colitis (UC).
Materials and Methods: Following the induction of ulcerative colitis in all groups [colitis (C), mesenchymal (MSC) and MSC + estradiol (MSC + EST)] except the control, in 2 groups MSC and MSC + EST respectively: 200 µl supernatant of $2x10^6$ mesenchymal stem cells and 200 µl supernatant of $2x10^6$ mesenchymal stem cells treated with 17-bED were injected 3 times during 10 days (IP). After the experimental period, Tissue specimens were collected and following the tissue passage and section, the slides were stained by H&E for histopathological evaluations.
Results: The results obtained from the colon tissue of the C group showed the presence of many inflammatory cells in the mucous layer (the space between the crypts), many eosinophilic cells in the sub-epithelial, collagenous colitis in the mucosa, severe vascular congestion in the submucosa and as well as the loss of normal structure of the epithelial cells. In the mucosal layer of MSC groups and especially MSC + EST, inflammatory cells were seen scattered along with a decrease in eosinophil cells and collagenous colitis. Mild to moderate vascular congestion and loss of epithelial cells and crypts were reported in some areas.
Conclusion: The present study showed the improvement of histopathological symptoms caused by the induction of UC following the use of mesenchymal stem cell supernatant, especially in MSC + EST group.
Keywords: Histopathology, Mesenchymal Stem Cells, 17-Beta Estradiol

Ps-45: Evaluation The Levels of Inflammatory Cytokines TNF-α, IL-1 and IL-6 in Acetic Acid Induced Ulcerative Colitis in Rats Treated with Condition Medium of Mesenchymal Cells Treated with 17-Beta Estradiol

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Objective: Ulcerative colitis (UC) is a form of inflammatory bowel disease with increased levels of inflammatory cytokines. The present study aims to investigate the ameliorating effects of condition medium of mesenchymal cells (CMm) treated with 17-beta estradiol (17-bED) on the level of inflammatory cytokines in an animal model of UC.
Materials and Methods: In this study, 40 male Wistar rats (150-200 g) were randomly placed into 4 groups; control, colitis (C), mesenchyme (MSC) and MSC+estradiol (MSC+EST). MSCs obtained from the bone marrow of male Wistar rats were cultured in the presence of 100 nM 17-bED for 24 hours, and UC was induced using 4% acetic acid in all groups except the control group. In the MSC and MSC+EST groups, after UC induction, respectively: 200 µl CMm obtained from $2x10^6$ cells and 200 µl CMm obtained from $2×10^6$ cells treated with 17-bED were injected intraperitoneally 3 times during 10 days. At the end, the rats were sacrificed and the mRNA expression of cytokines, including TNF-α, IL-1 and IL-6 in homogenous colon tissue samples was performed by RT-PCR method.
Results: The results showed that the highest and lowest levels of mRNA expression of cytokines were respectively in colitis and control groups, which had significant differences with each other and with other groups (P<0.05). Also, the obtained results indicate that the cell groups (MSC and MSC+EST) significantly reduce the levels of TNF-α, Il-1 and Il-6 compared to the Colitis group and even the MSC+EST group shows a significant decrease compared to the MSC group (P<0.05).
Conclusion: The present study showed the effect of CMm and especially CMm containing 17-beta estradiol in reducing the levels of inflammatory factors.
Keywords: Condition Medium, Inflammatory Cytokine, Ulcerative Colitis,17-Beta Estradiol,

Ps-46: Ameliorating Role of Condition Medium of Mesenchymal Cells Treated With 17-Beta Estradiol on The Oxidative Factors in An Experimental Model of Ulcerative Colitis

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Objective: Application of the condition medium obtained from the culture of mesenchymal stem cells accelerates the regeneration process of damaged tissue by reducing the levels of oxidants. The present study aimed to the role of condition medium of mesenchymal cells treated with 17-beta estradiol (17-BED) on the levels of myeloperoxidase (MPO) and nitric oxide (NO) in acetic acid induced ulcerative colitis (UC) in male rats.
Materials and Methods: MSCs obtained from the bone marrow of male Wistar rats were cultured in the presence of 100 nM 17-bED for 24 hours, and UC was induced using 4% acetic acid in colitis(C), mesenchyme (MSC) and MSC+estradiol (MSC+EST) groups. After UC induction, in the MSC and MSC+EST groups, respectively: 200 µl CMm obtained from $2×10^6$ cells and 200 µl CMm obtained from 2x106 cells treated with 17-bED were injected intraperitoneally (3 times during 10 days). After 10 days, the rats were sacrificed and the levels of MPO and NO in homogenous colon tissue samples was per-

formed.
Results: The results of this study showed a significant increase in MPO and NO in the C group compared to other groups ($P<0.05$) that MSC and MSC+EST groups were able to create a significant decrease ($P<0.05$). Also, the level of NO in the MSC+EST group was significantly reduced compared to the MSC group ($P<0.05$).
Conclusion: This study showed that CMm and CMm containing 17-beta estradiol decreased MPO and NO by ameliorating the levels of oxidants.
Keywords: Myeloperoxidase, Nitric Oxide, 17-Beta Estradiol, Ulcerative Colitis

Ps-47: Gene Expression Evaluation to Investigate Novel Hub Gene in Cardiomyocyte Differentiation

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Objective: Heart dysfunction is one of the most problems in our country. To solve that we have many traditional approaches, such as heart transplantation; however, this therapeutic way has some challenges.
Materials and Methods: So, the cellular therapy used alternative approaches in this way. The problem in this novel wat lacks of molecular information about the cardiomyocyte differentiation. To this end, we used bulk-RNA-seq data to gain differential expression genes (DEGs) by GEO2R software. In addition, to find protein-protein interaction network authors utilize STRING database via Cytoscape software. besides these programs, we used the CentiScape package to find hub genes. In the current study, we used GSE18514 data to indicate 4624 DEGs. To understand more about the protein interaction PPIs network constructed
Results: The ACTB node reported as main hub gene in cardiomyocyte differentiation from stem cells for the first time in this study.
Conclusion: The results of this study could be used to produce cardiomyocyte tissue as part of heart muscle, which increases the chance of cell therapy approaches in future.
Keywords: Bioinformatics, Cardiomyocyte, Cell Therapy, Differentiation, Heart Failure

Ps-48: Using Transgenic Zebrafish Model to Evaluation of Hyperglycemia Effects

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Objective: Diabetes mellitus (DM) is characterized by sustained elevation of systemic glucose levels. Three major complications of DM, collectively termed triopathy, comprise diabetic neuropathy, nephropathy, and retinopathy. Hyperglycemia, a key diagnostic parameter in both types of diabetes, significantly contributes to these complications, notably impairing sensory and/or motor functions affecting 50 percent of patients with this metabolic disorder. While a cohort of diabetic animal models has been established to investigate diabetes-related nerve disorders, the emergence of the zebrafish (Danio rerio) as a potent new model organism in central nervous system (CNS) disease modeling offers distinct advantages in this area. This research, conducted at the Kawakami zebrafish lab at the National Institute of Genetics (NIG, Japan), aimed to assess the impact of hyperglycemia on the nervous system and pancreas, utilizing two transgenic zebrafish lines with green fluorescent protein (GFP) expression in the entire nervous system [SAGFF(LF)19B] and pancreatic cells (gSA2AGFF323A).
Materials and Methods: Hyperglycemia was induced in transgenic larvae at 5 days post-fertilization by exposure to a 120 mM glucose solution for 5 days. Subsequently, the GFP area of transgenic larvae was quantified using Fiji software and statistically analyzed using Prism software in both treatment and control groups.
Results: The results revealed a significant decrease in the GFP area in treated larvae compared to the control group. For the SAGFF(LF)19B line (n= 15, ***P=0.0002) and the gSA2AGFF323A line (n= 30, **P =0.0053), this decrease was statistically significant.
Conclusion: Prior studies have highlighted that hyperglycemia in zebrafish larvae leads to motor axon defasciculation, disruptions in perineurial glial sheath formation, reduced myelination of motor axons, and mislocalization of sensory neurons. This study further demonstrates that a 5-day exposure of larvae to a 120 mM glucose solution results in damage to the nervous system and impairs pancreas development.
Keywords: Diabetes Mellitus, Diabetic Neuropathy, Hyperglycemia, Transgenic Zebrafish,

Ps-49: Rapid Synthesis of Silver Nanoparticles Using Henna Extract for Induced Apoptosis on Retinoblastoma Cell Line

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Objective: This study aims to rapidly synthesize silver nanoparticles (AgNPs) using Henna extract to trigger apoptosis in retinoblastoma cells, a common intraocular cancer in children. Green synthesis methods are utilized for their reproducibility, biocompatibility, and lack of toxicity, with Henna extract selected for its medicinal properties.
Materials and Methods: AgNPs are synthesized with Henna leaf extract and a 0.01 molar silver nitrate solution. Physicochemical properties of the AgNPs, including size, surface charge, and morphology, are characterized using techniques such as spectrophotometry, energy-dispersive X-ray spectroscopy (EDS), dynamic light scattering (DLS), and field emission scanning electron microscopy (FESEM). Toxicity tests are performed on retinoblastoma (Y79) and retinal pigment epithelia (ARPE19) cells to evaluate cellular viability, apoptosis and mitochondrial function with flowcytometry used to assess apoptotic and necrotic cell percentages.

Results: Successful synthesis of AgNPs is confirmed by a peak at 400 nm in spectrophotometric analysis. DLS indicates an average size of 103 nanometers with a surface charge of -43.5 mV. EDS verifies 50% silver content in the nanoparticles, while FESEM images show spherical nanoparticles. Toxicity tests on the Y79 cancer cell line demonstrate significantly higher toxicity at 100 mg/ml compared to Henna extract or silver solution alone, with no impact on healthy ARPE19 cells. Staining and apoptosis assays reveal cytotoxic effects on cancer cells, resulting in around 40% cell death versus <10% in healthy cells. The AgNPs induce mitochondrial dysfunction and nuclear abnormalities in cancer cells, with 15% undergoing necrosis and 23% experiencing late-stage apoptosis per flow cytometry analysis.
Conclusion: Green-synthesized AgNPs exhibit stabilized, eco-friendly properties with improved anticancer effects. Cytotoxicity assessments on the Y79 cell line suggest the potential of AgNPs as an effective cancer treatment delivery method. Further research in this area could lead to enhanced strategies for tackling difficult tumors.
Keywords: Green Synthesis of Nanoparticles, Retinoblastoma, Henna Plant, Silver Nanoparticles, Y79 Cell Line

Ps-50: Enhancing Dental Pulp Stem Cell Potential: Chick Embryo Extract Preconditioning For Neurotherapeutic Applictions

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Objective: Dental pulp stem cells (DPSCs) are promising candidates for cell-based therapies in neurodegenerative diseases, exhibiting potential for neural lineage differentiation and promoting tissue regeneration through paracrine effects. However, challenges such as limited *ex vivo* expansion and inefficient differentiation into neural lineages hinder their clinical application. In the present study, we aimed to explore the impact of chick embryo extract (CEE) preconditioning on the properties of DPSCs during *in vitro* cultivation, aiming to enhance their suitability for neurotherapeutic applications.
Materials and Methods: DPSCS were isolated from the pulp region of rat teeth and cultured in media supplemented with either 10% fetal bovine serum (FBS) alone or combined with 10% CEE. The study assessed cell multipotency, morphological changes, and gene expression associated with paracrine effects across both experimental conditions.
Results: Our results showed that CEE supplementation can preserve the rate of DPSCS multipotency. The preconditioned stem cells acquire neural-like morphology with longer neurites. Furthermore, CEE preconditioning upregulates the expression of brain-derived neurotrophic factor (BDNF), glial cell line-derived neurotrophic factor (GDNF), and vascular endothelial growth factor (VEGF).
Conclusion: These outcomes indicate that CEE preconditioning could equip DPSCs with beneficial attributes during *in vitro* culture, potentially improving their efficacy in treating neurodegenerative disorders. This approach represents a significant advancement towards leveraging the full therapeutic potential of dental pulp stem cells in neurotherapeutic applications.
Keywords: Chick Embryo Extract, Dental Pulp Stem Cells, Neurotrophic Factors, Preconditioning

Ps-51: Neuroprotective Effect of Hair Follicle Stem Cell-Derived Conditioned Medium in An Aschemia Model of Astrocytes

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Objective: Hair follicle stem cells (HFSCs) have emerged as promising candidates for cell-based therapy in stroke preclinical studies. The therapeutic potential of HFSCs towards neuroprotection is essentially based on their paracrine effects, referred as secretome. Secretome contains various biologically active molecules including growth factors, chemokines, and exosomes. The paracrine effect of HFSCs is suggested as a key mechanism contributing to the protection and restoration of brain cells after ischemic injury. Astrocytes play pivotal roles during brain ischemia, and understanding their role in HFSC-mediated protection against ischemic injury is crucial. This study investigates HFSC-derived secretome in an astrocyte ischemia model to assess its protective effects and underlying mechanisms for potential stroke therapy.
Materials and Methods: This study utilized an *in vitro* model of ischemic stroke using primary astrocyte cultures exposed to 24 hours oxygen-glucose deprivation (OGD) conditions. Subsequently, OGD-induced astrocytes were treated with HFSC conditioned medium (HFSC-CM) for 48 hours to create an environment rich in paracrine factors. The neuroprotective effect of HFSC-CM on injured astrocytes was evaluated using the MTT assay, apoptosis flow cytometry, and qRT-PCR.
Results: The HFSC-CM mitigated cell death and apoptosis in OGD-induced astrocytes. Additionally, the HFSC-CM reduced the mRNA expression levels of pro-inflammatory cytokines IL-6, IL-1β, and TNF-α compared to the injured cells. Furthermore, it upregulated the mRNA levels of neurotrophic factors BDNF, and VEGF after OGD in astrocytes.
Conclusion: These findings suggest that the reparative effects of the secretome are associated with astrocyte neuroprotection, anti-inflammatory properties, and anti-apoptotic effects. The neuroprotective effect of HFSC secretome may be associated with the upregulation of neurotrophic and angiogenic factors. The restored astrocytes create a conducive environment for repair, thereby expediting the recovery of impaired brain function. This study provided preclinical evidence for further use of HFSC secretome in stroke therapy to improve the treatment outcome of patients who suffered from ischemic stroke.
Keywords: Astrocyte, Hair-Follicle Stem Cell, Ischemic Stroke Model, Neuroprotection, Oxygen-Glucose Deprivation

Ps-52: Novel Approached for Identification Prognostic Biomarker for Osteosarcoma base on Data-Mining and scRNA-Seq

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Objective: Osteosarcoma is considered one of the most severe types of bone cancer, with a 5-year survival rate as low as 40% in younger age groups. The lack of validated methods for prognosing this disease leads to individuals suffering and dying due to insufficient biomarkers. Therefore, identifying the most effective and patient-specific biomarkers associated with prognosis could significantly enhance their quality of life and overall health.
Materials and Methods: For this goal, an extensive literature search was carried out in the Scopus database (https://www.scopus.com/home.uri) to pinpoint relevant prior studies centered on discovering osteosarcoma biomarkers using bioinformatics workflows. Initially, 832 pertinent articles were identified through this process. Subsequent refinement and analysis reduced this figure to 99 articles that satisfied the inclusion criteria for our study. The search queries and filtering criteria primarily focused on articles containing keywords such as “osteosarcoma”, “biomarker”, and “prognosis”. Through data mining, all potential markers mentioned in each article were extracted and organized into terms pertinent to osteosarcoma. Finally, a list was compiled featuring related terms (38 terms) and genes. For future analysis and identification of the most effective prognostic markers for osteosarcoma, a single-cell RNA sequencing (scRNA-seq) dataset encompassing six osteosarcoma patients was retrieved from the NCBI Gene Expression Omnibus (GEO) database. During this process, all data underwent analysis using the Seurat package within R Studio (R version 4.3.3, https://www.r-project.org/). Cells exhibiting expressions below 300 or above 7000 were excluded, as were those with a mitochondrial percentage exceeding 15%. Subsequently, variable features were identified in all normalized samples using the "FindVariableFeature" function to pinpoint the top 2000 genes and the initial 30 principal components (PCAs) for cluster identification with a resolution of 0.5. Integration of all samples and the removal of batch effects were achieved utilizing the "rPCA" integration pipeline within the Seurat package, followed by cluster annotation. Ultimately, our investigation focused on establishing the relationship between each marker's expression in our integrated samples to discover an optimal biomarker panel associated with the osteosarcoma disease term through the utilization of scRNA-seq and data-mining techniques. Remarkably, we identified a significant relationship between specific biomarkers, such as “DCN” and “CD74” with the prognosis of osteosarcoma.
Results: Results were merged into material and methods.
Conclusion: Based on our findings, we propose DCN and CD74 as the best biomarkers for assessing osteosarcoma prognosis. However, *in vitro* validation assessments are needed for future results and to propose the best biomarker panel for the prognosis of osteosarcoma.
Keywords: Osteosarcoma, Biomarker, scRNA-seq, R Studio, Prognosis

Ps-53: Multi-Omics Approach Identifies ACADM as a Biomarker for Head and Neck Cancer

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Objective: Head and neck squamous cell carcinoma (HNSCC) ranks as the seventh most prevalent cancer globally and is increasingly associated with poor lifestyle choices. Despite advancements in therapeutic strategies, the 5-year survival rate for early-stage (I–II) HNSCC patients ranges from 70–90%, whereas it declines to approximately 40% for those with advanced stages (III–IV). This disparity highlights the heterogeneity inherent in HNSCC. The identification of reliable diagnostic and prognostic biomarkers could markedly enhance life expectancy and overall patient health.
Materials and Methods: In this context, analysis of RNA expression data was conducted to evaluate differentially expressed genes (DEGs). A binomial deep learning algorithm was employed to ascertain genes with notable variability in expression. The study also included comprehensive evaluations through protein-protein interaction (PPI) networks, the construction of Receiver Operating Characteristic (ROC) curves, and single-cell RNA sequencing (scRNA-seq) assessments.
Results: The findings indicate a strong association of ACADM with the carcinogenic processes in HNSCC, underscoring its potential as a significant biomarker. These insights pave the way for improved diagnostic precision and therapeutic outcomes, ultimately enhancing patient management and survival rates in HNSCC. Additionally, integrating ACADM expression patterns with clinical data may offer novel insights into the stratification of patient risk groups, enabling more personalized treatment approaches.
Conclusion: Lastly, ongoing research into the modulation of ACADM activity could lead to the development of targeted therapies that specifically exploit metabolic vulnerabilities in HNSCC, offering a promising avenue for enhancing treatment efficacy and reducing recurrence rates.
Keywords: Biomarker, Deep Learning, HNSCC, Prognosis, scRNA-seq,

Ps-54: Resveratrol-loaded PLA-PEG nanoparticles trigger apoptosis in 4T1 Breast Cancer Cells

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Objective: Researchers continue to grapple with the challenge of effectively treating cancer while minimizing the adverse effects associated with current therapies. In light of this, there is a growing need to investigate the potential of natural sources to provide anticancer antioxidants as an alternative to chemo

drugs. Resveratrol is a natural polyphenol found in grape skins, plums, peanuts, and bilberries. It has various therapeutic effects, including modulation of cell-signaling pathways, antioxidant properties, anti-aging attributes, anti-inflammatory effects, anticancer properties, and neuroprotective qualities. Polymeric nanoparticles are highly effective as nanocarriers due to their outstanding properties, including biocompatibility, biodegradability, non-toxicity, non-immunogenicity, and the ability to control drug delivery. The present study aimed to evaluate the effects of Resveratrol-loaded PLA-PEG nanoparticles [polylactic acid–poly (ethylene glycol)] on the cell death mechanism by increasing the expression of pro-inflammatory genes.

Materials and Methods: 4T1 cell line was cultured in Dulbecco's modified Eagle's medium (DMEM) and supplemented with 10% fetal bovine serum and 100 ug/ml penicillin/streptomycin. Cell lines were kept in a CO^2 incubator at 5% CO^2 and 37° C temperatures. 4T1 cells were treated with Resveratrol-loaded PLA-PEG nanoparticles (0, 100 µM) for 1, 12, and 24 hours. Cells were trypsinized and frozen to perform quantitative RT-PCR experiments

Results: Real-time polymerase chain reaction (PCR) analysis showed that Resveratrol-loaded PLA-PEG nanoparticles significantly increased the transcriptional levels of IL-1β and TNF-α after 24 hours. However, no significant changes were observed in the expression of IL-1B and TNF-a mRNA levels after treatment with Resveratrol-loaded PLA-PEG nanoparticles for 12 hours.

Conclusion: Finally, our study found that the Resveratrol-loaded PLA-PEG nanoparticles caused apoptosis in the breast cancer cell line, effectively eliminating 4T1 cells. This indicates that PLA–PEG polymeric nanoparticles can be used as a reliable method to release resveratrol and control the growth of breast cancer cells.

Keywords: Cancer, PLA-PEG Nanoparticles, Resveratrol, 4T1

Ps-55: Cytotoxic Effect of Gold Nanoparticles-Conjugated Thymoquinone in Human MDA-MB-231 Breast Cancer Cells

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Objective: Breast cancer is the most prevalent form of cancer in women worldwide. Detecting it in its early stages and identifying potential drugs to combat multi-drug resistant metastatic breast cancers offers the potential for improved treatment options and extended life expectancy. Following the selection of the phytochemicals, attention is then directed towards the delivery systems that possess inert properties and are capable of effectively transporting drugs to specific cancer sites. Extensive research has been conducted by scientists on various delivery systems, including nanoparticles such as silver and gold, as well as liposomes. These investigations have been carried out both in controlled *in vitro* and within living organisms, to enhance therapeutic efficacy against different types of cancers, as well as metastatic and drug-resistant tumors. Among the nanoparticles, gold nanoparticles (AuNPs) have been widely utilized as drug delivery systems due to their ease of synthesis, large surface area, ability to be easily functionalized, and high biocompatibility. This new formulation shows promise in effectively delivering hydrophobic chemotherapeutic to tumors for cancer treatment.

Materials and Methods: The study aimed to assess the anti-metastatic effects of thymoquinone in combination with gold nanoparticles (AuNP-thymoquinone) in *in vitro* models (MDA-MB 231).

Results: The combination treatments of AuNP-thymoquinone were highly effective in the apoptosis of breast cancer cells (MDA MB 231) *in vitro*. In-depth studies on gene expression showed that these anti-cancer effects were linked to the suppression of *VEGF* and *HOXB9* genes, while the overexpression of the apoptotic *Caspase-3* gene was observed.

Conclusion: The findings suggest that administering gold-conjugated thymoquinone formulations could potentially impact the effectiveness of chemotherapy. This research is strongly backed by data obtained from cell-based experiments and molecular investigations.

Keywords: Breast Cancer Cell Lines (MDA-MB 231), Gold Nanoparticles, Thymoquinone

Ps-56: Effects of Mesenchymal Stem Cell Transplantation on Major Adverse Cardiovascular Events and Cardiac Function Indices in Patients with Chronic Heart Failure: A Systematic Review and Meta Analysis of Randomized Controlled Trials

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Objective: Trials on efficacy of mesenchymal stem cells (MSCs) transplantation in heart failure (HF) have been controversial. This study was conducted to investigate whether MSCs transplantation after HF could improve clinical outcomes and myocardial indices.

Materials and Methods: Using systematic approach, electronic databases were searched for randomized controlled trials (RCTs) until July 2023. Outcomes of interest included clinical outcomes and myocardial function indices. Using random-effects method, relative risk (RR) , mean difference (MD) and corresponding 95% confidence intervals (CI) were pooled.

Results: In Seventeen RCTs with 1684 patients (927 intervention, 757 control) the mortality RR was 0.78 (0.62; 0.99) in the MSC group compared to controls. Rehospitalization only decreased significantly in autologous MSC group [RR= 0.67 (0.49; 0.90)]. LVEF significantly increased among those receiving MSC [MD= 3.38 (1.89; 4.87)]. LVESV [MD= -9.14 (-13.25; -5.03)], LVEDV [MD= -8.34 (-13.41; -3.27)], and scar size [standardized MD= -0.32 (-0.60; -0.05)] significantly decreased. NYHA class [MD= -0.19 (-0.34; -0.06)], and MLHFQ [MD= -11.55 (-16.77; -6.33)] significantly decreased and 6-minute walk test significantly improved [MD = 36.86 (11.22; 62.50)] in the MSC group. Heart failure cause did not influence outcomes. However, trials with the autologous source of cells, doses less than 100 million cells, and intracoronary injection performed significantly better in some outcomes.

Conclusion: Transplantation of MSCs for HF patients may reduce all-cause mortality and improve clinical condition. Moreover, this treatment would improve left ventricular function indi-

ces and reduce scar size.
Keywords: Cardiomyopathy, Heart Failure, Meta-Analysis, Mesenchymal Stem Cells, Randomized Controlled Trials

Ps-57: Effectiveness of Stem Cell Transplantation Therapy Using Mesenchymal Stem Cells Versus Bone Marrow-Derived Mononuclear Cells in Heart Failure Patients: A Meta-analysis of Randomized Controlled Trials

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Objective: Mesenchymal stem cells (MSCs) and bone marrow-derived mononuclear cells (BM-MNCs) transplantation have emerged as heart failure therapies. However, clear comparison between them has never been established. This meta-analysis aimed to compare the cardiovascular outcomes of MSCs and BM-MNCs therapies.
Materials and Methods: Pertinent studies in online databases were systematically searched to find eligible randomized trials on heart failure patients receiving either MSCs or BMMNCs. Clinical outcomes and echocardiographic indices were included. Random-effects approach was used to combine the relative risk (RR) or mean difference (MD) along their respective 95% confidence intervals (CI).
Results: A total of 32 studies with 2487 patients (1356 in intervention, 1131 in control group) were included. Stem cell therapy did not yield reduced risk of MACE [RR 0.83 (0.64; 1.06)] but could decrease the risk of all-cause death by 21% [RR 0.79 (0.64; 0.97)] and marginally decrease rehospitalization by 24% [RR 0.76 (0.59; 1.00)] compared with placebo with no between-subgroup differences (P>0.05). Transplantation of stem cells resulted in a significant increase in LVEF [MD 3.00 (1.80; 4.20)] and LVESV [MD -8.02 (-13.24; -2.80)] but not LVEDV [MD -4.11 (-10.35; 2.12)] with no difference between stem cells (P>0.05).
Conclusion: Stem cell therapy with BMMNCs and MSCs demonstrated efficacy in improving LVEF and LVESV and also decrease rehospitalization and all-cause death although no change in MACE was found. Both types of stem cells are efficient in patients with heart failure with no significant difference between cells.
Keywords: Bone Marrow-Derived Mononuclear Cells, Mesenchymal Stem Cells, Heart Failure, Randomized Controlled Trials, Meta-Analysis

Ps-58: Cell Spheroids Derived from Human Keratinocytes and Fibroblasts as Biological Models

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Objective: Current skin models *in vitro*, including skin equivalents, skin-on-chip and organoids, reproduce the architecture and cellular composition of native skin well. However, their fabrication methods are time-consuming and laborious. This has led to the search for new approaches to human skin modeling. One such approach involves the use of cell spheroids. In this study, we aimed to investigate the effect of formation conditions on the structure and properties of keratinocyte and fibroblast multicellular spheroids in order to determine optimal co-culture conditions for achieving a histotypic structure.
Materials and Methods: Four experimental groups of spheroids were formed: two groups of monospheroids composed of HaCaT keratinocytes or 977hTERT fibroblasts, and two groups of heterospheroids derived from co-cultures of these cells. Spheroids were analyzed using immunocytochemistry (ICC), quantitative real-time polymerase chain reaction (qRT-PCR), western blotting, biomechanical tests, phase-contrast and confocal microscopy.
Results: Diameter measurements have shown that fibroblast monospheroids increased in size, while the diameters of other groups gradually decreased. Reactivation experiments have demonstrated that heterospheroids spread out on a substrate more actively than monospheroids. Biomechanical tests revealed differences in stiffness between groups of mono- and heterospheroids. Localization of protein markers (keratin 19, ZO-1, vimentin, collagen I) and epidermal differentiation analysis showed that heterospheroids formed by layering keratinocytes on a fibroblast core have a more precise epidermal-dermal architecture and more differentiated keratinocytes compared to heterospheroids obtained by mixing two cell types.
Conclusion: Heterospheroids formed by layering can be used as an *in vitro* skin models, while heterospheroids obtained by mixing are better suited for studying cell interactions within the spheroid. This work was supported by the Russian Science Foundation (23-25-00503).
Keywords: Skin Models, Spheroids, Co-Culture

Ps-59: Novel identification of two THBS1 and RUNX2 hub genes in neuron differentiation

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Objective: Spinal cords Injuries are the most important reason of movement disorders. Based on the slow rate of proliferation of nerve cells, this disorder still untreatable. In this perusal, the authors attempted to understand more about the molecular behaviors via high-throughput array techniques such as microarrays.
Materials and Methods: In addition, our evaluation has indicated 3008 differential expressed genes (DEGs) from GSE27334 via GEO2R software, which demonstrated differential molecular alteration during neural differentiation from P19 stem cells through Retinoic Acid (RA). In order to understand protein behavior, we used STRING database from Cytoscape software to construct the protein-protein interaction (PPIs) network. Which showed 3209 nodes and 28266 edges. Moreover, to find the genes that have most interaction from PPIs, we utilized CentiScape plug-in that reported 30 hub genes within higher than or equal 138 interactions.
Results: Among that two THBS1 and RUNX2 reported for the first time in the current study as novel hub genes, which could be important during the neural differentiation for the novel thera-

peutic approaches.
Conclusion: Among that two THBS1 and RUNX2 reported for the first time in the current study as novel hub genes, which could be important during the neural differentiation for the novel therapeutic approaches.
Keywords: Hub Gene, Cell Therapy, Bioinformatics, Neural Differentiation, RNA-seq

Ps-60: Optimizing the Chimera Formation in Chicken Embryos Using Human Pluripotent Stem Cells

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Objective: The formation of chimeras is an important technique for evaluating the developmental potential of human pluripotent stem cells (hPSCs). Our previous research indicated that the chicken embryo is a suitable host due to its developmental similarity to the human embryo at the primitive streak stage. However, we encountered challenges associated with the lengthy process of transferring the fertilized egg to the surrogate eggshell, leading to increased embryo mortality. To address this issue, we suggest a new approach to enhance human-chicken chimera formation.
Materials and Methods: We injected primed Royan H6 cells at a rate of 3000-5000 cells in 3 microliters into HH4 stage embryos. Instead of using the previous method, where a surrogate eggshell was used to inject the cells from the wide top, fertilized eggs were placed on their side for at least 1 hour and injected the cells directly into that side. After 7 days, we examined the morphology and survival of the embryos, as well as the presence of human cells using the STEM121 antibody.
Results: After comparing the old and new methods, we found that increased efficiency in chimera formation reduced fetal mortality during cell injection into the primitive streak after 7 days and decreased the number of consumed chick embryos. Although we observed abnormalities in the morphology of some chick chimera, staining with STEM121 antibody revealed the presence of hPSCs.
Conclusion: Our approach enhances precision, simplifies handling, and speeds up chimera generation. Furthermore, we validated the reproducibility of chimera formation in chick embryos using hPSCs.
Keywords: Chick Embryo, Interspecies Chimera, Human Pluripotent Stem Cell, ,

Ps-61: Effect of Calligonum Plane Eetract on Colonization Olonization and Reactive Oxygen Species Production in Sheep Spermatogonial Stem Cells

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Objective: The balance between self-renewal and differentiation of spermatogonial stem cells (SSCs) in the testicles of adult species causes the creation of regular cycles,the most important results of which are spermatogenesis and the possibility of potential fertility
Materials and Methods: The testes of immature Afshari lambs were first washed with 70% tincture of iodide.Then mechanical digestion was performed by strile scissors.in two stages of enzymatic digestion the collagenase IV, hyaluronidase II and trypsin enzymes were used.The samples assigned into four groups. i. The control ii. H_2O_2, iii. Calligonum iv. Calligonum+H_2O_2. Flow cytometry was used to measure the amount of reactive oxygen species(ROS)inside the cell.The mRNA genes expression of BAX, BCL2 in all groups were measured.An inverted microscope equipped was used to evaluate the number of colonies on days 5,14,and 21of culture
Results: The number of spermatogonia colonies in the control and Calligonum groups was higher than the other two groups ($P\leq0.05$) on the 5thand 14thdays of culture.The highest and lowest number of spermatogonial colonies were observed in Calligonum and H_2O_2 groups($P\leq0.05$),respectively on the 21st day.The lowest and highest percentage of cells containing ROS, BAX expression,and BAX/BCL2 ratio were observed in Calligonum and H_2O_2 groups ($P\leq0.05$), the highest amount of BCL2 expression was in Calligonum group ($P\leq0.05$)
Conclusion: The use of Calligonum in the culture improves the colonization rate in sheep spermatogonial stem cells and controls the amount of ROS production rate in these cells.The expression of BCL2 and BAX genes,as inhibitory and compelling factors of apoptosis,also increases and decreases in the presence of Calligonum
Keywords: Spermatogonia, Calligonum, Colonization, ROS, Sheep

Ps-62: Janus-Like Collagen Membrane: A New Platform in The Urethra Restoration

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Objective: Collagen-based materials, especially membranes, are widely used in the biomedical field due to their mechanical properties and suture retention ability, which makes them useful for surgical procedures, particularly urethroplasty. There are two main approaches to produce collagen-based membranes: decellularization and reconstruction. We have developed an innovative modification of the collagen electrophoretic deposition method to produce robustly no-defect membranes that can be industrially scaled. This study aims to show its applicability to restore the urethra using a rabbit as a model.
Materials and Methods: Bovine Achilles tendons obtained fresh frozen from local farms and were used as a source of type I collagen. The tendons were treated with NaCl, homogenized, hydrolyzed, and purified. The resulting suspension was precipitated electrophoretically in an electrochemical cell separated by a semi-permeable barrier. The obtained membranes were dried, crosslinked, and mechanically perforated. Soviet Chinchilla rabbits (n=15) were chosen as an animal model. The experiments were carried out in accordance with international regulations.

Results: The high membrane's biocompatibility was proven by the Live/Dead assay using 3T3 cells and MSCs. *In vivo* experiments showed the complete epithelialization by the urothelium at day 45 with implant's resorption and replacement by own tissues. α-SMA staining revealed the absence of fibrosis. Urethrocystography showed no signs of stenosis by day 180. In contrast, the control group had the marked stenosis without the mucosal regeneration.
Conclusion: The developed approach allows creating implants applicable in urethroplasty and possessing appropriate mechanical properties. The membranes' application was efficient and ensured high epithelization level without the stricture formation.
Keywords: Tissue Engineering, Urethra, Collagen, Urethroplasty, Mechanics

Ps-63: Modulation of The Inflammatory Response of Macrophages by Mesenchymal Stromal Cells-Derived Exosomes and Matrix-Bound Nanovesicles

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Objective: The ability to control the process of inflammation for chronic inflammation, for example, osteoarthritis, is one of the most important challenge in the field of regenerative medicine. There is a need for therapies that are able to modulate the immune response the inflammatory process without having systemic side effects. Extracellular vesicles [matrix-bound nanovesicles (MBV) and exosomes] have shown the ability to modulate the inflammation process by changing the polarization of macrophages in the direction of the anti-inflammatory phenotype.
Materials and Methods: The study used EVs derived from the secretions and ECM of human umbilical cord mesenchymal stromal cells (U-MSCs). Both types of EVs were added to macrophages together with polarization inducers in the M1 (IFN-γ+LPS) and M2 (IL-4) phenotypes. The effects of EVs on the macrophage polarization were evaluated using ELISA and qRT-polymerase chain reaction (PCR). Production of reactive oxygen species (ROS) production in macrophages was evaluated by luminol-dependent chemiluminescence (CL).
Results: ELISA and qRT-PCR showed that МИV and exosomes reduced the production of inflammatory cytokine TNF-α and IL-6 in M1 macrophages compared with control cells receiving only IFN-γ+LPS. QRT-PCR showed that MBV increased the expression level of CD-206 of the M2 polarization marker to a greater extent than exosomes. In addition, in the MBV group there was a more pronounced decrease in the expression of the NF-kB subunit responsible for inflammatory activation of macrophages. Incubation of macrophages with EVs caused a decrease in ROS production by M1 macrophages compared with control cells, which was confirmed by the CL method.
Conclusion: MBV and exosomes of the U-MSCs inhibit the pro-inflammatory activity of M1 macrophages, enhance M2 anti-inflammatory polarization of macrophages and the radical-generating activity of macrophages, which shows their potential use as therapy for diseases caused by chronic inflammation. This research was funded by grant from Russian Science Foundation (# 23-25-00497, rscf.ru/en/project/23-25-00497/).
Keywords: Extracellular Vesicles, Matrix-Bound Nanovesicles, Macrophage Polarisation, ,

Ps-64: Biofabrication of Urethral Equivalent From Spheroids of The Buccal Epithelium and Mesenchymal Stromal Cells

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Objective: Currently, diverse scaffolds with immobilized cells formed with 3D bioprinting are widely used in regenerative medicine. 3D cellular spheroids serve as building blocks for the biofabrication, owing to the cell-cell, cells-matrix interconnections, as well as nutrient and oxygen gradients. These spheroids help preserve cell viability during bioprinting by reducing stress and mimicking microenvironments. Primary cell cultures sourced from human tissues present a promising resource due to the potential for personalized medicine. Extended genitourinary stricture stands out as a prevalent affliction causing considerable discomfort in affected individuals. Innovative methods using tissue equivalents can be effective treatments alongside traditional urethroplasty techniques. In urethral biofabrication, integrating multilayered epithelium and stroma mimics human tissue complexity. The main goal was complex characterization of spheroids from buccal epithelium and MSCs and formation of bilayered bioequivalent from epithelial and mesenchymal cells by 3D-bioprinting.
Materials and Methods: Buccal epithelium and multipotent mesenchymal stromal cells (MSCs) were isolated from explants of human oral cavity tissues, characterised using flow cytometry. Spheroids were formed using 3D petri dish agarose plates (MicroTissue, USA). Bioequivalents were created using a 3D CELLINK BioX bioprinter (CELLINK, Sweden) based on fibrin hydrogel.
Results: Comprehensive characterization of the spheroid's cytoskeleton, extracellular matrix components morphology, mechanical properties, and expression profiles of key markers, was performed. Cell viability in spheroids was assessed, along with their ability to reorganize on plastic surfaces and in a fibrin-based hydrogel. Distinct phenotypes of spheroids, representing epithelial and mesenchymal lineages, were successfully generated. Buccal epithelium-derived spheroids exhibited a mixed marker expression profile, indicative of both epithelial and mesenchymal cell characteristics. MSC-derived spheroids predominantly displayed mesenchymal features and demonstrated faster compaction and reactivation abilities. Bilayer bioequivalents were constructed using epithelial and mesenchymal cells in conjunction with fibrin-based bioinks. During maturation, epithelial spheroids form a cell layer on the upper surface, while mesenchymal spheroids create a dense layer at the base.

Conclusion: The study was supported by the Russian Science Foundation (№ 23-15-00481).
Keywords: Spheroids, 3D-Bioprinting, Biofabrication, Buccal Epithelium, MSCs

Ps-65: The Effect of Conditioned Medium from Bone marrow-derived Mesenchymal Stem Cells on The Prefrontal Cortex in Type 2 Diabetic Rats

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Objective: Diabetes leads to the damage of prefrontal cortex neurons and causes behavioral disorders. It has been suggested that conditioned medium (CM) derived from bone marrow mesenchymal stem cells (BM-MSCs) can improve the complications caused by diabetes. This study examines the effect of CM from BM-MSCs on the prefrontal cortex of type 2 diabetes model rats.
Materials and Methods: 40 Male Wistar rats (8 wk, 200-250 gr), were randomly divided into following groups: control, diabetes, diabetes+Dulbecco's Modified Eagle Medium (DMEM), diabetes+CM, and pretreatment. To induce diabetes, 120 mg/kg nicotinamide and 15 minutes later 65 mg/kg STZ (streptozotocin) were injected intraperitoneally. One week later, 250 µl of CM (or DMEM) was injected intravenously to group 3 and 4. Pretreatment group received CM two weeks before diabetic induction and also for three weeks afterwards. Two months after the first CM injection, the rats were examined by Elevated Plus Maze behavioral test to investigate anxiety-like behavior. Histopathological examination was done by Nissl staining and pyknotic neurons were counted. The expression of Bcl-2 and Bax genes were evaluated by quantitative real-time polymerase chain reaction. The biochemical tests including total antioxidant capacity, and malondialdehyde were assessed. Finally, data was analyzed by SPSS software and ANOVA test.
Results: The present study showed that the induction of diabetes in rats increased the number of pyknotic neurons ($P<0.0001$), Bax mRNA expression ($P<0.05$) and malondialdehyde level ($P<0.05$) in diabetic rats. The CM administration decreased the number of pyknotic neurons ($P<0.001$) and increased the expression of Bcl2 and total antioxidant capacity ($P<0.01$). Also, the CM injection decreases anxiety-like behavior in rats ($P<0.001$).
Conclusion: These findings suggest that CM produced from BM-MSCs may be valuable for therapeutic approaches in diabetes and reduce its negative effects.
Keywords: Bone Marrow Mesenchymal Stem Cells, Conditioned Medium, Prefrontal Cortex, Streptozotocin, Apoptosis

Ps-66: Viral Fusion Peptide Stimulated The Interaction of Engineered Exosomes with Breast Cancer Stem Cells

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Objective: Currently, numerous researches have been concentrated to increase the therapeutic effects of extracellular-vesicles, especially exosomes for the alleviation of several diseases. It has been indicated that systemically injected exosomes can distribute easily in all biofluids, resulting in the increase of off-target effects. Thus, attempt should be concentrated to increase the uptake rate of exosomes by the target cells. In this research, engineered exosomes were produced using viral fusion peptide, using covalent interaction
Materials and Methods: MDA-MB-231 breast cancer stem cell exosomes were isolated using consequential centrifugation step and decorated with respiratory syncytial virus (RSV) fusion peptide using the click chemistry. The engineered exosomes were assessed using DLS analysis in terms of hydrodynamic diameter. To assess the reciprocal interaction of engineered exosomes with endothelial cells, surface plasma resonance (SPR) biosensing method was performed. MDA-MB-231 cells were cultured on gold-coated SPR chip to yield single cell layer and exposed to naïve and engineered exosomes at flow rate of 15 µl/minute for 5 minutes.
Results: Data indicated the increase of exosome diameter,135 vs. 315 nm, after the addition of viral peptide coincided with the elevation of zeta potential values from -10 to -1 mV. SPR analysis confirmed the increase of RU values between the engineered exosomes compared to the naïve exosomes. These data indicate the increase of physical contact between the circulating exosomes with the of single MDA-MB-231 monolayer.
Conclusion: Decoration of exosomes with viral fusion peptide can be used for the increase of therapeutic efficiency and delivery efficiency of exosomes to the target cells.
Keywords: Breast Cancer Stem Cells, Exosomes, Viral Fusion Peptide, Physical Interaction, On-Target Efficiency

Ps-67: Evaluation Of Anti-Aging Effects Of Human Placenta Extract On Senescent Cell Model

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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-epithelization, 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 (H_2O_2)-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 (H_2O_2)

for a 2-hour duration. The optimal dose was determined using the MTS test. Furthermore, we assessed the expression levels of aging-related genes, including P53 and P21, to validate the cell senescent model. HDFs were initially treated with an optimal dose of HPE for 24 hours, followed by exposure to H_2O_2. After a total treatment duration of 26 hours (24 hours of HPE treatment and 2 hours of H_2O_2 exposure), we assessed the expression levels of aging-related genes and compared them to those in the established model.
Results: In the presence of oxidative stress, HPE demonstrated a significant increase in cellular viability. Moreover, it not only enhanced cell proliferation but also mitigated apoptotic induction. HPE effectively reduced the expression of senescence marker genes.
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, H_2O_2, Anti-Aging

Ps-68: Re-purposing Clove Oil in Ovarian Cancer Treatment: A Multi-Dimensional Approach Involving Bulk RNA-Seq and scRNA-Seq

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Objective: Ovarian cancer (OC) is currently the fifth leading cause of cancer-related deaths among women, with approximately 140,000 fatalities globally per year. To improve the prognosis of OC patients, novel therapeutic approaches are essential . Cancer stem cells (CSCs) are integral to ovarian cancer's entire development process, including initiation, metastatic progression, therapeutic resistance, and disease recurrence. Thus, targeted therapy, particularly against ovarian cancer stem cells (OCSCs), is expected to be more effective and less toxic, potentially improving patient survival and reducing tumor relapse.
Materials and Methods: Our initial analysis utilized GSE13237 dataset, from NCBI gene expression omnibus (GEO), which includes data from 11 pairs of primary and metastatic Ovarian Cancer tumors. We employed RNA-seq pipeline,"DESeq2" package, setting a threshold of $p < 0.05$ and $|logFC| > 1$ to identify highly variable genes. This yielded 2134 significant genes. Subsequently, using the "clusterProfile" package and David online enrichment tool for KEGG, we repurposed "clove oil"—a biotech-type, reliever of neuropathic pain used for toothache and mild pain—as a potential agent targeting *COL1A1* gene. This gene plays a significant role in metastasis and stem cell regulatory pathways. To ensure accuracy, we further analyzed scRNA-seq datasets GSE184880 and GSE158937, comprising 8 samples (5 healthy and 3 high-grade serous metastatic OC) with "Seurat" package in R studio.
Results: The results significantly enriched the *COL1A1* gene in the cancer cell cluster, providing clear evidence of its association with OCSCs. We have found out that there is a significant relationship between "*COL1A1*" expression and "Clove oil".
Conclusion: By understanding the genetic underpinnings and potential therapeutic targets like the COL1A1 gene, we can pave the way for more effective and personalized treatments for ovarian cancer, offering hope for improved outcomes.
Keywords: Ovarian Cancer, Cancer Stem Cells, Clove Oil, Collagen Type I Alpha 1 (COL1A1)

Ps-69: The Potential of Oncolytic Virus as A Therapeutic Strategy for Glioblastoma Treatment (2D and 3D Model)

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Objective: This study aimed to evaluate the cytotoxic effects of the oncolytic virus Onco-VV-TT on glioblastoma (GB) cell lines and its impact on glioblastoma stem cell (GSC) properties. Specifically, the study examined the virus's ability to inhibit cell migration and colonization, and analyzed the temporal dynamics of virus-induced cell death and its penetration into spheroids. The findings aim to highlight the potential of Onco-VV-TT as a therapeutic agent for GB treatment.
Materials and Methods: Human (U251 and U87) and rat (C6) GB cell lines were treated with various multiplicities of infection (MOI) of Onco-VV-TT for 24, 48, and 72 hours to assess cell viability and proliferation. Colony formation and wound healing assays were performed to evaluate the inhibition of cell migration. Flow cytometry (FACS) was used to determine the type of cell death induced by Onco-VV-TT. Spheroids were infected with the virus, and their viability and virus penetration were assessed over 72 hours using confocal microscopy. The ability of spheroids to reattach post-virus infection was also evaluated.
Results: Onco-VV-TT significantly reduced cell viability and proliferation of GB cell lines in a dose-dependent manner. At an MOI of 1, the virus effectively decreased colony formation in U251, U87, and C6 cell lines, with the most pronounced effect observed in U251 cells. Wound healing and colony formation assays confirmed the inhibition of cell migration and colony formation following Onco-VV-TT infection.
Conclusion: Onco-VV-TT demonstrated significant cytotoxic effects on GB cell lines, inhibiting GSC properties, cell migration, and colonization. The virus induced a temporal progression of cell death and effectively penetrated spheroids, resulting in substantial cell death. These findings suggest that Onco-VV-TT holds promise as a therapeutic agent for GB treatment.

Keywords: Oncolytic Virus, Glioblastoma, Cancer Stem Cell, Immunoviro Therapy

Ps-70: Astrocyte Exosomes; Novel Therapeutic Source in Central Nervous System

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Objective: Among different glial cell within the central nervous system, astrocytes are valid cell component involved in maintaining brain homeostasis and neurogenesis. It has been thought that extracellular vesicles (EVs), especially exosomes, can regulate inter astrocyte-neuron communication in a paracrine manner. In this study, we performed protocol for the isolation and enrichment of mouse fetus astrocyte exosomes for possible application in biomedical fields.
Materials and Methods: Cerebral cortexes of fetal mouse were sampled and cut into small pieces without enzymatic solution. The cell suspensions were transferred into culture flasks and allowed astrocyte population attached the bottom surface while gentle agitating. The supernatants containing non-astrocyte cells were discarded. Upon 80-90% confluence, astrocytes were subjected to starvation in FBS-free culture medium to collect the exosomes. After consequential centrifugation steps, the isolated exosomes were characterized and immunophenotyped using DLS, SEM, and western blotting.
Results: Wester blotting revealed the existence of tetraspanins such as CD63, CD81, and TSG101 in exosome pellets. SEM images confirmed heterogenous round-shape particles. DLS analysis indicated hydrodynamic diameters of ~336 nm with and zeta potential of -32 mV, indicating typical exosome physicochemical properties.
Conclusion: Taken together, primary astrocyte exosomes can be isolated and pooled from astrocytes for different regenerative purposes.
Keywords: Mouse, Cerebral Cortex, Astrocytes, Exosomes, Biomedical Application

Ps-71: The Effect of Biocompatibility Properties of Electrospun Polycaprolactone-Gelatin Scaffold Containing Layered Double Hydroxide Nanoparticels on L929 Mouse Fibroblast Cells

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Objective: Nanofibrous scaffolds provide cells with an environment similar to the body's extracellular matrix, which is effective on cell morphology, adhesion, proliferation and function. The present study aims to investigate the biocompatibility properties of polycaprolactone and gelatin electrospun scaffold containing LDH nanoparticles on L929 mouse fibroblast cells.
Materials and Methods: In this research, LDH nanoparticles were synthesized by co-precipitation method. Using the electrospinning method, a scaffold made of polycaprolactone and gelatin with optimal nanoclay 1% by weight was made. The synthesized nanoparticles were evaluated by X-ray diffraction (XRD) and SEM. 20 thousand L929 fibroblast cells were planted on the scaffolds for 3 to 5 days. Then they were placed in alcohols of different percentages to dehydrate the scaffolds. After drying the scaffolds, a scanning electron microscope (SEM) was used to characterize and examine the stabilized cells. MTT was used to evaluate the toxicity of the scaffolds. Cell evaluations were evaluated by examining adhesion, viability, and proliferation of L929 cells
Results: By adding LDH, the fiber diameter decreased. The biocompatibility of the PCL-GEL-LDH scaffold was investigated after the culture of L929 mouse fibroblast cells with the MTT test, and the results showed that the survival rate of the cells cultured on it increased compared to PCL-GEL. Also, SEM images showed better interaction and proliferation of L929 cells on PCL-Gel-LDH than PCL-GEL.
Conclusion: Adding LDH to PCL-GEL nanofibers has a positive effect on cell adhesion and viability.
Keywords: Polycaprolactone-Gelatin, Double Layered Hydroxide Nanoparticles, Mouse Fibroblast Cells

Ps-72: The Effect of Wound Dressing Containing Polycaprolactone-Gelatin-Layered Double Hydroxide Carrying The Drug On Wound Healing In Guinea Pigs

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Objective: Nanofibrous scaffolds containing layered double hydroxide nanoparticles are very important in drug delivery for healing skin wounds. The purpose of this study is to investigate the effect of PCL-GEL-LDH wound dressing containing the drug 4-methyl-7-hydroxycoumarin on wound healing in guinea pig skin tissue.
Materials and Methods: In this research, a scaffold made of polycaprolactone and gelatin with 1% by weight optimized nanoclay containing coumarin drug was made using electrospinning method. The synthesized nanofibers were evaluated by X-ray diffraction (XRD) and SEM. There male guinea pigs were used to make the animal model. Three square wounds with dimensions of 2 x 2 cm were created in the skin of the back surface of each guinea pig. In each guinea pig, the wounds were divided into 3 groups: wounds without receiving any treatment, wounds with polymer, and wounds with drug-carrying polymer-nanoparticles. The wound surface and wound healing rate in the studied groups were checked on days 7 and 14 after treatment using H&E staining and Image J and SPSS software.
Results: In examining the wound surface on the 7th and 14th day, the smallest and largest wound surface was observed in the polymer-nanoparticle-coumarin, polymer-nanoparticle, and untreated wound groups, respectively. In examining the percentage of wound healing on days 7 and 14, the highest percentage of healing was observed in the polymer-nanoparticle-coumarin

group, polymer-nanoparticle, and untreated wound, respectively, and there was a significant difference between these 3 groups on day 14.
Conclusion: The wound dressing containing polymer-nanoparticles carrying the drug coumarin had a good compatibility with the skin wound in guinea pigs and had a better effect on accelerating the healing of skin wounds in guinea pigs than the polymer without LDH carrying the drug.
Keywords: Polymer-Nanoparticle Wound Dressing, Coumarin Drug, Guinea Pig Skin Wound

Ps-73: Gabapentin Reduced Osteo-Differentiation of Bone Marrow Mesenchymal Stem Cells Via Down-Regulation of Related Genes

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Objective: Gabapentin (GP) as an analog of GABA, is the most commonly used medicine to treat neurological pain. Studies revealed continuous application of GP causes bone mass density reduction in patients. The present study aimed to investigate its effect on the osteogenic differentiation of bone marrow mesenchymal stem (BMSCs) which are responsible for producing osteoblasts.
Materials and Methods: Rat BMSCs were extracted and treated with different concentrations of GP for 21 days, and then 10-8 and 10-4 M were selected for further study in osteogenic media. Matrix production was investigated using alizarin red quantitative analysis and calcium level estimation. In addition, the activity of alkaline phosphatase (ALP) and expression of osteo-related genes including BMP 2 and 7, RUNX2, osteocalcin, Alp, and collagen 1 were determined.
Results: Statistical analysis showed that the matrix production by differentiated BMSCs reduced significantly ($P<0.05$) in a dose-dependent manner after treatment with GP. In addition, the activity of ALP reduced significantly and the expression of all the investigated genes also reduced significantly ($P<0.05$) in the presence of GP.
Conclusion: GP reduces the osteo-differentiation of BMSCs by affecting related genes which finally causes the reduction of bone matrix production.
Keywords: Gabapentin, BMSCs, Osteogenic Differentiation, Gene Expression,

Ps-74: Resveratrol-Coated Chitosan Mats Promote Angio-Genesis for Enhanced Wound Healing In Animal Model

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Objective: Growing incidences of chronic wounds recommend the development of optimal therapeutic wound dressings. Electrospun nanofibers have been considered to show potential wound healing properties when accompanied with other wound dressing materials. This study aimed to explore the potential role of Chitosan (CS) nanofibrous mats coated with resveratrol (RS) as an antioxidant and pro-angiogenic agent in rat model of skin wound healing.
Materials and Methods: Electrospun chitosan/polyethylene oxide (PEO) nanofibers were prepared using electrospinning technology and coated by 0.05 and 0.1 mg.ml resveratrol named as (CS/RS 0.05) and (CS/RS 0.1), respectively. The scaffolds were characterized physio-chemically such as *in vitro* release study, TGA, FTIR spectroscopy analysis, biodegradability and human dermal fibroblasts seeding assay. The scaffold subsequently used *in vivo* as a skin substitutes on a rat skin wound model.
Results: *In vitro* tests revealed that all scaffolds promoted cell adhesion and proliferation. However, more cell viability was observed in CS/RS 0.1 scaffold. The biocompatibility of the scaffolds was validated by MTT assay, and the results did not show any toxic effects on human dermal fibroblasts. It was observed that RS coated scaffolds had the ability to release RS in a controlled manner. In *in vivo* tests CS/RS 0.1 scaffold had the greatest impact on the healing process by improving the neodermis formation and modulated inflammation in wound granulation tissue. Histological analysis revealed enhanced VEGF expression, epithelialization and increased depth of wound granulation tissue.
Conclusion: The RS coated CS/PEO nanofibrous scaffold accelerates wound healing and may be useful as a dressing for cell transfer and clinical skin regeneration
Keywords: Chitosan, Resveratrol, Electrospinning, Angiogenesis, Wound Healing

Ps-75: Investigating The Immunogenic Properties of Artificial Insulin Producing Cells

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Objective: Immune rejection presents a substantial challenge in diabetes treatment by stem cell transplantation. The current work investigated the immunological features of insulin-producing cells (IPCs) generated from adipose-derived mesenchymal stem cells (ADSCs) both *in vitro* and *in vivo*.
Materials and Methods: The research was carried out at Ahvaz Jundishapur University of Medical Sciences in 2023. ADSCs were derived from rat adipose tissues and differentiated into IPCs. The control group consisted of undifferentiated ADSCs. The amount of secreted insulin was measured using ELISA. The *in vitro* expression of MHC-I and MHC-II, CD40, and CD80 by IPCs was assessed using Western blot analysis. The *in vivo* study was performed on ten male diabetic rats. The experimental group received 107 IPCs in the peritoneal cavity. The control group received 10 7 Un-differentiated ADSC. After 4 hours, the expression of CD3a and CD45 by immune cells collected from the peritoneal cavity was measured using Flow cytometry.
Results: The differentiated cells secreted much higher amounts of insulin than the control group. ($P=0.004$). IPCs exhibited higher expression of MHC-I and MHC-II, CD40, and CD80.

(P= 0.02, P= 0.008, P= 0.07, P= 0.02 respectively). The experimental group showed higher levels of CD3a and CD45 expression than the control group. (P= 0.07, P= 0.04 respectively).
Conclusion: Functional IPCs generated by ADSC differentiation exhibited immunogenic activity both *in vitro* and *in vivo*. As a result, immune-modulating strategies are required for the effective transplantation of the differentiated IPCs generated in our study.
Keywords: Adipose-Derived Mesenchymal Stem Cell, Insulin, Cell Differentiation, Immunogenicity

Ps-76: Gabapentin Effects Osteo-Differentiation of Bone Marrow Mesenchymal Stem Cells Due to The Induction of Oxidative Stress

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Objective: Gabapentin (GP) is an anticonvulsant medicine prescribed to treat neurological complications. Studies showed that GP causes osteoporosis in patients following continuous consumption. We investigated the oxidative stress induced by GP on bone marrow mesenchymal stem cells (BMSCs) differentiated to osteoblasts *in vitro*.
Materials and Methods: Rat BMSCs were treated with different concentrations of BP and then concentrations of 10-8 and 10-4 M were selected for further analysis. Osteogenic differentiation, cell viability, nuclear and cytoplasm morphology, total protein concentration, malondialdehyde (MDA) level, total antioxidant capacity (TAC), and antioxidant enzymes (CAT and SOD) activity was determined. In addition, the expression of oxidative stress-related genes (NFkB and Nrf2) was estimated using real-time polymerase chain reaction (PCR).
Results: Alizarin red staining showed osteogenic differentiation of BMSCs was reduced significantly following treatment with selected dose of GP. In addition, GP reduced the cell viability and total protein concentration and decreased the nuclear diameter and cytoplasm area of the treated cells significantly ($P<0.05$) compared to the control one. It was shown that GP caused elevation of MDA and reduced the TCA as well as the activity of the antioxidant enzymes. It was revealed that the expression of NFkB increased and Nrf2 decreased after treatment with the selected dose of GP.
Conclusion: GP reduces cell viability and changes the morphology of osteo-differentiation of BMSCs via induction of oxidative stress.
Keywords: Gabapentin, Morphology, Oxidative Stress, Gene Expression,

Ps-77: Anti-Tumor Effect of Lapatinib In Combination with Standard Care In Patient Derived Bladder Cancer Organoid (PDO)

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Objective: Bladder Cancer (BLCa) inter-patient heterogeneity is the primary cause of treatment failure, suggesting that patients could benefit from a more personalized treatment approach. Organoid as an aggregation of adult stem cell, progenitor of cells or induced pluripotent stem cell can recapitulate organ function in miniature. Patient derived organoids have been used as a preclinical model to predict or personalize treatment.
Materials and Methods: In our study, we stablish PDO culture from different stage of BLC of 30 patients. Patient-derived organoid characterized for ability of grow, sub culturing capability, long term proliferation potential, size, viability and also expression of specific bladder organoid markers by RT-PCR. The organoid forming efficiency was evaluated by confocal microscopy for CK20, GATA3a, CK20, UPK III and proliferation marker (KI67). Then the generated model was used for early stage of drug screening in different concentration of Lapatinib in compare with standard care.
Results: Our drug screening pipeline is implemented using PDOs, testing standard-of-care and FDA-approved compounds for other tumors. We successfully establish and culture organoids from NMIBC and MIBC that recapitulate the PTs' key aspects. Integrative analysis of drug response profiles with matched PDO analysis is used to determine enrichment thresholds for candidate markers of therapy response and resistance. Finally, the result indicate synergic effect of lapatinib in combination with cisplatin and gemcitabine and in compare with cisplatin and gemcitabine (or either alone) on the well stablished preclinical model of bladder tumor organoids.
Conclusion: In summary, with this study, we have generated a unique model of BLCa organoids which retain cancer heterogeneity and can be employed in drug-sensitive screens. Moreover, we showed the dose dependent behavior of Lapatinib in combination with standard care and the specific concentration with synergic effect significantly inhibit the proliferation and growth tumor organoids.
Keywords: Bladder Tumor, Organoid, Drug Screening, Disease Modeling, Lapatinib

Ps-78: Development of an Optimized Protocol for Generating Knockout Cancer Cell Lines Using The CRISPR/Cas9 System, with Emphasis on Transient Transfection

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Objective: The clustered regularly interspaced short palindromic repeats (CRISPR) system, a bacterial immunity mechanism against phage and other invading factors, has instigated a profound revolution in eukaryotic genome editing over the last dec-

ade. This system empowers researchers to conduct intricate genetic modifications such as gene knockout, knock-in, activation, repression, and single-base editing. Compared to conventional gene editing methods, CRISPR/Cas9 offers distinct advantages: affordability, exceptional efficiency, remarkable accuracy, and unparalleled user-friendliness.
Materials and Methods: Here, we develop an optimized approach for generating knockout cancer cell lines using a plasmid vector and nonviral delivery method. In this paper, we present a detailed nine-step instruction set encompassing various precise procedures. This includes employing a lipid nanoparticle-based delivery strategy, leveraging robust bioinformatics tools, conducting indispensable assays, isolating monoclonal cells via limiting dilution, and validating biallelic gene knockout through sequencing analysis.
Results: These steps collectively enable the creation of knockout cell lines within ten weeks. We successfully created several new generations of colorectal cancer cell lines with monoallelic and biallelic epithelial cell adhesion molecule (EpCAM) gene knockout by using this method.
Conclusion: Consequently, by employing our method, which contains stepwise instructions and comprehensive troubleshooting recommendations, researchers with limited laboratory equipment and minimal funding, especially for researchers undertaking CRISPR projects for the first time, can produce knockout cell lines efficiently to significantly enhance their investigations in cancer research, unravel disease mechanisms, and pave the way for potential therapeutic interventions.
Keywords: CRISPR, Gene Knockout, Cancer Cell Lines, Transient Transfection, Monoclonal Cell Population

Ps-79: Scalable Generation of Functional Retinal Pigmented Epithelial Cells from Human Embryonic Stem Cells in Stirred Suspension Bioreactor Technology

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Objective: Human embryonic stem cells possess the capability to differentiate into a variety of cell types, including retinal pigmented epithelium cells (RPEs), showing potential for addressing conditions such as age-related macular degeneration. The progress in utilizing human pluripotent stem cells in animal models of retinal failure highlights the necessity for practical protocols to produce functional RPE cells at a larger scale.
Materials and Methods: In this experimental investigation, we introduce a technique for growing functional RPE cells from human embryonic stem cells in a scalable stirred-suspension bioreactor. The differentiation process entailed the utilization of Noggin, retinoic acid, and Shh to prompt neural ectoderm and RPE specification. The characterization of the RPEs was conducted through Real-time polymerase chain reaction (PCR), immunofluorescent staining, flow cytometry, and a phagocytosis assay.
Results: Over a span of 60 days, hESCs effectively transitioned into RPE cells. The isolated pigmented cells exhibited a hexagonal morphology reminiscent of mature native RPEs. By day 56, the differentiated cells displayed elevated expression levels of crucial RPE markers like Mitf, RPE65, Bestrophin, and ZO-1, with RPE65 expression surpassing 70% in suspension culture.
Conclusion: A comparison with adherent conditions, where the expression stood at 40%, indicates a notable improvement in RPE cell culturing efficiency in suspension culture. This scalable enrichment approach establishes a fresh framework for producing functional RPEs, providing a plentiful cell source for applications such as drug screening, disease modeling, and potential cell replacement therapies for individuals affected by retinal degenerative diseases.
Keywords: Retinal Pigmented Epithelium Cells, Scale-Up Differentiation, Stirred Suspension Bioreactor, Human Embryonic Stem Cells

Ps-80: Turmerone-Loaded Niosomes Inhibit Proliferation and EMT in Hepatocellular Carcinoma *In Vitro* Models

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Objective: Hepatocellular carcinoma (HCC) is the most frequent primary liver malignancy and the fourth most lethal cancer. Current HCC therapies have different challenges, including tumor recurrence, drug resistance, and low bioavailability of the drugs. Recently, nanodrug delivery systems such as non-ionic surfactant-based nanocarriers (also known as niosomes) have attracted much attention in cancer treatment due to their appropriate encapsulation, stability, bioavailability, and release properties.
Materials and Methods: In this study, turmerone-loaded niosmes (tur-nio) were synthesized using the thin film hydration method. Niosome characteristics such as size, polydispersity index (PDI), and Zeta potential were assessed with dynamic light scattering (DLS). In addition, the storage stability of niosomes was examined at 4 °C and 25 °C using DLS. The anti-cancer effects of tur-nio were investigated through performing proliferation, apoptosis, cell cycle, and scratch assays on Huh7 and Hep3B cells. Additionally, the effect of tur-nio on the expression of genes related to epithelial-mesenchymal transition (EMT), and apoptosis examined.
Results: DLS analysis indicated that niosomes were completely stable at 4 °C for two months. Tur-nio significantly inhibited proliferation of Huh7 and Hep3B cells. Flowcytometry analysis indicated that tur-nio treatment efficiently induced apoptosis and cell cycle arrest in Huh7 and Hep3B cells. Furthermore, the scratch assay showed that in tur-nio treated cells, migration capacity was significantly inhibited. EMT related genes were down regulated as well. The expression level of N-cadherin and Vimentin was significantly decreased in tur-nio treated cells in comparison with the control group. In addition, tur-nio treatment increased the expression level of E-cadherin. Gene analysis assays indicated that viability of Tur-nio cells were significantly decreased.

Conclusion: Conclusion: This study showed that turmerone-loaded niosomes have anti-cancer properties and could be used as a promising device for HCC treatment. In addition, these results suggest that niosomes could be a novel candidate for drug delivery in HCC.
Keywords: Niosome, Cancer, HCC, Nanotechnology,

Ps-81: Advanced Tissue Clearing Technique for High-Resolution Visualization of Ocular Structures: A Comparative Study Using FACT Protocol

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Objective: It is essential to have high-resolution visualization of the physiological ocular structure and cellular interactions to better understand and treat eye diseases. In this study, we aim to achieve this by utilizing advanced tissue clearing techniques, specifically employing the Freeof-Acrylamide Clearing Tissue (FACT) method.
Materials and Methods: In this study, we established the FACT protocol on eye tissues using C57BL/6 mice and transgenic zebra fish. We examined five groups: 1) Intact, 2) Treated with 10% H_2O_2 (hydrogen peroxide) for 3 hours at 55°C, 3) Treated with 2% SDS (Sodium dodecyl sulfate) for 48 hours at 37°C, 4) Treated with 2% SDS for 72 hours at 37°C, and 5) Treated with 4% SDS for 48 hours at 37°C. We conducted retinal morphometry through cryostat sectioning and DAPI staining, followed by image analysis using ImageJ. Transgenic zebra fish were used to assess the impact of FACT on GFP.
Results: Comparison between the 2% and 4% SDS-treated groups revealed a significant decrease in the outer nuclear layer length in the 2% group (p value <0.0001). However, no significant morphological changes were observed in the retinal layers treated with 4% SDS for 48 hours at 37°C compared to the H_2O_2-treated and Intact samples. Notably, the FACT protocol did not alter the retinal layers in zebra fish, and fluorescence remained preserved.
Conclusion: In conclusion, the FACT protocol demonstrated varying effects of SDS treatments on ocular tissue morphology, with the 4% SDS group showing minimal alterations. The preservation of fluorescence in zebra fish retina post-clearing underscores the potential of FACT in maintaining cellular integrity for enhanced visualization of ocular structures.
Keywords: Tissue Clearing, Ocular Morphology, Sodium Dodecyl Sulfate, Setinal Integrity, Fluorescence Preservation

Ps-82: HCC Cells Decreased Hepatic Characteristics After Exposing to Fibrotic Liver ECM-Derived Microparticles in 3D Liver Micro-Tissues

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Objective: Hepatocellular carcinoma (HCC), the third most fatal cancer worldwide, accounts for 164.9% increase in their mortality by the end of 2045 in Iran. HCC mostly occurs in the background of liver fibrosis and cirrhosis. Fibrosis is characterized by excessive accumulation, and remodeling of the extracellular matrix (ECM) which is followed by the development of hepatic nodular regenerative hyperplasia in liver cirrhosis. The incidence of hyperplasia is associated with the altered microenvironment in inflammation-driven liver fibrosis, and the substantial changes in ECM might contribute to this regenerative nodule. This study aims to identify whether alteration in biochemical compounds of fibrotic ECM can regulate the hepatic maturation in HCC cells in biomimetic platform.
Materials and Methods: Initially, to produce ECM, rat liver tissues from both control (normal) and carbon tetrachloride (CCl4)-induced liver fibrosis were decellularized using sodium dodecyl sulfate (SDS) and Triton X-100. The extracellular matrix (ECM) obtained from the decellularized tissues was processed into microparticles through the water-in-oil emulsion technique. These microparticles were then integrated into three-dimensional liver biomimetic micro-tissues (MTs) composed of Huh-7 cells, human umbilical vein endothelial cells (HUVECs), and LX-2 cells. The liver microtissues were cultured ex-vivo for 14 days and their gene expression profile, and protein secretions were analyzed.
Results: The results indicated that the fibrotic matrix from CCl4-treated rat livers significantly decreased the expression of hepatic maturation genes *HNF4A*, *ALB*, and *CYP3A4* in the MTs. Moreover, MTs incorporating the fibrotic matrix showed a marked increase in the secretion of alpha-fetoprotein.
Conclusion: Our findings suggest a regulatory role for the fibrotic matrix in accelerating dedifferentiation, which could potentially facilitate the progression of malignancy in the liver.
Keywords: Hepatocellular Carcinoma, Liver Fibrosis, Extracellular Matrix, Liver Micro-Tissue, Hepatic Differentiation

Ps-83: The Study of The Modulation of Collagen Alignment By Stem Cells in Mechanical Properties of Wound Healing

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Objective: Recently, the use of random flaps has become widespread in the field of plastic surgery. With the clinical application of random flaps in plastic surgery, skin defects can be improved in terms of aesthetics and functionality. With the development of regenerative medicine, stem cell therapy is a promising way to increase regeneration and accelerate tissue healing in chronic wounds.
Materials and Methods: Twenty male albino Wistar rats with an average weight of 250-300 g were used in this research. Also, five rats of the same breed weighing 30 to 40 g were used to extract bone marrow cells. The animals were divided into two healthy groups of without therapeutic intervention and with therapeutic intervention of stem cell injection so that there were

ten animals in each group. In both groups, day zero was the day of surgery and all the 20 animals underwent surgery. A random skin flap measuring 3 x 8 cm was created in the back area of the animals and the results were checked on the 14th day in the transitional area.
Results: BMMSCs injection increased the survival level and decreased the necrotic wound level, but this improvement was not statistically significant. Also, the injection of BMMSCs improved the biomechanical properties of wound healing, the increase of which was statistically significant except for energy absorption, but in terms of the synthesis, content, and arrangement of collagen fibrils, the injection of BMMSCs was ineffective. In the untreated group, there was more collagen and more organized arrangement in collagen fibrils.
Conclusion: Local injection of BMMSCs did not significantly increase the survival level of random skin flap, but improved the wound healing process. Also, the injection of BMMSCs did not increase collagen content and improve the arrangement of collagen fibrils, but significantly improved the biomechanical properties of the wound.
Keywords: Random Skin Flap, Bone Marrow-Derived Mesenchymal Stem Cells, Collagen, Wound Healing, Biomechanical Properties of Skin

Ps-84: Stem-Cell-Based Cancer Therapy with The Aid of "HYPOXIA"; The Common Feature of Mesenchymal Stem Cell Niche and Tumor Microenvironment

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Objective: Uncontrolled tumor cell division and proliferation cause a rapid increase in cell number and oxygen consumption, leading to a hypoxic condition in the tumor microenvironment (TME) of the most developing tumors (Pathologic Hypoxia). Similarly, the adipose tissue-derived mesenchymal stem cells (hASCs) reside in a healthy hypoxic niche (Physiologic Hypoxia). Studies have shown mesenchymal stem cells (MSCs) are inherently prone to migrate toward solid or developing tumors. Therefore, hypoxia, as a common feature of hASCs niche and TME, and tumor tropism could be used in cancer therapy that would introduce hypoxia-regulated-gene-engineered hASCs as a potential carrier to transfer and release the anti-tumor agents, specifically at the TME.
Materials and Methods: We investigated the effect of TME-mimicked hypoxia on a therapeutic transgene expression level in hASCs. For this purpose, a hypoxia-regulated therapeutic gene was constructed which contained the hypoxia-responsive elements (HRE) adjacent to the full cytomegalovirus (CMV) promoter, and cytosine deaminase::uracil phosphoribosyltransferase fusion gene (CD: UPRT), separated with an IRES2 from the enhanced green fluorescent protein gene (EGFP). Following the transfection of this recombinant construct into hASCs via lipofectamine, the cells were incubated in normoxia (21% O_2) and hypoxia (2-5% O_2) conditions. The expression level of the transgene was evaluated using fluorescence microscopy and flow cytometry.
Results: Although the transgene expression in hASCs was transient and had a significant toxicity effect on the cell population, the microscopic evaluation shows the transient expression of transgene (12 hours post-transfection) was significantly increased under hypoxic conditions while the low expression in normoxia.
Conclusion: This study indicates that the HRE results in higher transgene expression under hypoxia in hASCs. This result is optimistic for using engineered hASCs as a carrier for the antitumor therapeutic genes to exert their potential therapeutic effects after migration to the hypoxic TME.
Keywords: Mesenchymal Stem Cells, Cancer Therapy, Hypoxia

Ps-85: Associations between Endothelial Cell Biomarkers and GVHD

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Objective: Hematopoietic stem cell transplantation (HSCT) is a treatment for various hematologic disorders, but it can also lead to serious complications, such as graft-versus-host disease (GVHD). Elevated levels of coagulation factors indicate endothelial dysfunction, which can contribute to GVHD.
Materials and Methods: In this study, investigate the presence of enhanced endothelial dysfunction in patients who develop acute GvHD following allogeneic hematopoietic cell transplantation (allo-HCT). *In vitro* experiments were conducted where endothelial cells (ECs) were exposed to serum samples obtained from patients with aGvHD (n = 31) and without GvHD (NoGvHD, n = 13). plasma levels of various factors such as von willebrand factor VWF, TNF receptor 1 (TNFR1), soluble vascular cell adhesion molecule 1 (sVCAM-1), soluble intercellular adhesion molecule 1 (sICAM-1), and plasminogen activator inhibitor-1 (PAI-1) were measured. In the Immunofluorescence assay, ECs were cultured and treated with specific monoclonal antibodies against ICAM-1 and VCAM-1 and a polyclonal antibody against VWF. Finally, using a fluorescent microscope for capturing images. Furthermore, plasma levels of VWF, TNFR1, sICAM-1, PAI-1, and sVCAM-1 were quantified in individual patients using ELISA, and the results were statistically analyzed using Student's t test for paired data.
Results: VWF, sVCAM-1, PAI-1, ICAM-1 and TNFR1 exhibited significant increases in patients with GvHD.
Conclusion: Our findings suggest that ECs damage might be linked to GVHD. The relationship between endothelial cell activation and GvHD has been a topic of interest in recent research and have the potential to make a significant impact in the medical field and ultimately benefit those suffering from this challenging condition. Understanding how endothelial cell activation plays a role in the pathophysiology of GvHD could improve our knowledge of this condition. By focus on this relationship, further research may lead to improved diagnostic and treatment approaches for patients.
Keywords: Graft-Versus-Host Disease, Von Willebrand Factor, Endothelial Cell, Hematopoietic Stem Cell Transplantation

Ps-86: The Effect of Human Placenta Extract on Bone Differentiation of Mesenchymal Stem Cells

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Objective: Stem cell and molecular medicine
Materials and Methods: Mesenchymal stem cells with the ability to self-renewal and differentiate into various tissues were extracted and cultured from the umbilical cord. Then they were oriented towards ossification using a differentiation solution. Their bone differentiation was measured through alizarin red dye and this dye was also used to measure calcium density in the process of ossification. Human placenta extract was prepared in laboratory conditions and its protein content was checked. Differentiated bone cells were treated with human placenta extract, and the MTT test was performed on them to detect the absence of toxicity and cell viability, it was found that not only the placenta extract is not toxic, but also it caused the treatment of mesenchymal stem cells. Also, the differentiated cells that were treated with different concentrations of the extract were evaluated in terms of the amount of alkaline phosphatase and the amount of calcium, which are markers of ossification. Calcium deposits gradually increased with the effect of placenta extract. Then it was time to examine the osteocalcin gene, which is one of the genes at the end of the pathway. This gene plays a role in ossification differentiation, which was investigated by the real-time polymerase chain reaction (PCR) method, which in the dilution of 1 ml of placenta extract increased the osseous differentiation of stem cells compared to the control group, and the significant difference in the graph fully illustrates this issue
Results: Differentiated bone cells were treated with human placenta extract, and the MTT test was performed on them to detect the absence of toxicity and cell viability, it was found that not only the placenta extract is not toxic, but also it caused the treatment of mesenchymal stem cells. Also, the differentiated cells that were treated with different concentrations of the extract were evaluated in terms of the amount of alkaline phosphatase and the amount of calcium, which are markers of ossification. Calcium deposits gradually increased with the effect of placenta extract. Then it was time to examine the osteocalcin gene, which is one of the genes at the end of the pathway. This gene plays a role in ossification differentiation, which was investigated by the Real-time PCR method, which in the dilution of 1 ml of placenta extract increased the osseous differentiation of stem cells compared to the control group, and the significant difference in the graph fully illustrates this issue
Conclusion: So it can be concluded that despite the high ability of stem cells in treating diseases, placenta extract also increases the differentiation to ossification due to its many properties and the effect of treatment on stem cells so that the effect of these stem cells on treatment Diseases especially of the bone type will increase.
Keywords: Placenta Extract, Mesenchymal Stem Cells, Distinction, Umbilical Cord, Bone

Ps-87: Role of Autophagy in Homotypic Mitochondrial Transfer via Tunneling Nanotubes between Mesenchymal Stem Cells

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Objective: Here, the possible role of autophagy was investigated in mitochondrial donation via tunneling nanotubes (TNTs) between the human mesenchymal stem cell (MSCs) *in vitro*.
Materials and Methods: MSCs were treated with 15 μM Metformin (Met) and/or 3 μM 3-methyladenine (3-MA) for 48 hours. The generation of TNTs was monitored using bright-field and SEM images. The possible effects of autophagy modulation were assessed on mitochondrial membrane integrity. The crosstalk of autophagy signaling pathway was investigated with Wnt signaling pathway via polymerase chain reaction (PCR) array analysis. Using gas chromatography, the changes in fatty acid profile was also studies in different groups.
Results: The induction of autophagy via Met increased the TNT formation (number↑ and length↑) compared to 3-MA-treated group. Along with these changes, protein levels of Rab8 and p-FAK were diminished in 3-MA-treated MSCs with suppression of TNT formation. The stimulation/inhibition of autophagy can modulate the expression of different genes associated with Wnt signaling transduction pathway. Data revealed the increase of unsaturated fatty acids with the induction of autophagy compared to control and 3-MA-treated MSCs.
Conclusion: Autophagy modulation can influence TNT formation in MSCs coincided with homotypic transfer of intracellular compartments.
Keywords: Mesenchymal Stem Cells, Autophagy, Tunneling Nanotubes, Juxtacrine Interaction, Homotypic Transfer

Ps-88: Mitochondria-Incorporated Electroconductive Alginate-Based Hydrogel Promoted Myocardial Regeneration Via Vascularization In A Rat Model Of Myocardial Infarction

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Objective: Here, the angiogenesis properties of mesenchymal stem cell (MSC) mitochondria were investigated in a rat model of myocardial infarction
Materials and Methods: Mesenchymal stem cells were pretreated with mitochondria-induction compounds metformin (Met; 50 μM), and dichloroacetic acid (DCA; 40 μM). After the

isolation of mitochondria, the isolated particles were characterized and incorporated (~2 × 107 particles) inside the alginate (3%)-gelatin (1%) hydrogel containing 1 μM pyrrole in the presence of FeCl3. The physicochemical properties of the final composite were monitored using several assays such as FTIR, swelling, biodegradation, porosity tests, and SEM. Mitochondria-loaded hydrogels (~2 × 107 particles/100 μl) were injected into the border zone of infarcted myocardium induced by LAD ligation. After two weeks, rats were euthanized and mitochondrial uptake and angiogenesis status were monitored using histological examination.
Results: Data showed appropriate physicochemical (swelling rate, biodegradation, porosity) and cytocompatibility properties of alginate-gelatin pyrrole hydrogel evaluated by SEM, FTIR, and MTT assays. Flow cytometry analysis indicated high-rate purity and functionality of isolated mitochondria. Masson's Trichrome staining and ECG analysis indicated appropriate myocardial infarction in the control rats. Immunohistochemistry analysis showed the stimulation of angiogenesis in the infarcted area (vWF+ capillaries↑, and α-SMA+ arterioles↑) in rats that received mitochondria-loaded hydrogel compared to mitochondria and hydrogel groups ($P<0.05$). Data showed a significant increase in anterior wall thickness in the mitochondria-loaded hydrogel group ($P<0.05$).
Conclusion: Mitochondria-loaded hydrogels are suitable delivery platforms for the induction of angiogenesis and reduction of fibrosis in ischemic myocardium.
Keywords: Mesenchymal Stem Cells, Mitochondria, Hydrogel, Angiogenesis, Infarction

Ps-89: Human Placental Biomaterials Ameliorate Cancerous Phenotype in Hepatocellular Carcinome

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Objective: Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer and is responsible for the fourth cause of cancer-related deaths worldwide. It is predicted that by 2025, more than 1 million individuals will be influenced by HCC yearly; therefore, due to the insufficient methods of treatment, it represents a major health-care challenge globally. Recently, a new field in regenerative medicine led to the formation of Advanced Therapy Medicinal Products (ATMPs). Tissue-engineered medicinal products are a category of ATMPs. Placenta is a good source of extracellular matrix (ECM) and different biomaterials which are known for their antioxidative and anti-inflammatory properties. Hence, the objective of this study is to utilize the decellularized ECM of the human placenta in order to investigate the cancerous phenotype in HCC cells.
Materials and Methods: Hep-3B cells were treated with placental biomaterials. In order to find the preferable dosage, cell viability was evaluated using MTS after 24, and 48 hours treatment. Epithelial-mesenchymal transition (EMT) was assessed utilizing the mRNA expression of EMT markers. Cell migration was performed using wound-healing assay.
Results: Placental biomaterials ameliorated the cancerous phenotype in Hep-3B cell line. A reduction in cell viability was noticed after the treatment with placental biomaterials. Furthermore, we demonstrated an increase in CDH1, a decrease in CDH2 expression and switch cadherin in Hep-3B cell line.
Conclusion: Placental-derived biomaterials has shown a promising potential in attenuating cancerous phenotype such as cell viability, migration, and EMT process. It is hoped that with further studies placental-derived biomaterials can be used in amelioration and apoptosis of cancerous cells or might be a good candidate for combination therapies in HCC.
Keywords: Hepatocellular Carcinoma, Human Placental Biomaterials, Cell Migration, Epithelial-Mesenchymal Transition

Ps-90: Evaluation of The Effect of Saffron (Crocus Sativus L.) On The Viability Bone Marrow-Derived Mesenchymal Stem Cells of Rat (rBM-MSC)

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Objective: Medicinal plant extracts possess tremendous potential as agents for stem cell and regenerative therapy in the realm of public health, owing to their easy availability, cost-effectiveness, and least side effects. Saffron has been utilized in traditional medicine for an extensive period of time. Moreover, according to reports, saffron is utilized in the treatment of various diseases including cardiovascular disorders and cancer. Mesenchymal stem cells (MSCs) have exhibited remarkable immunomodulatory and antioxidant properties, thereby offering potential benefits in the treatment of various diseases. In the current study, we have evaluated the effects of saffron on the viability of MSCs, in order to clarify on the potential therapeutic effects of this compound in the context of stem cell-based therapies.
Materials and Methods: Bone marrow cells from rat's femurs and tibias were isolated and subsequently characterized by flow cytometry. The cytotoxicity of saffron on rBM- MSCs was accomplished through the utilization of the MTT assay. Following successful adherence of the cells to the culture plates, they were incubated for 24 hours and 37°C, during which they were treated with varying concentrations of saffron (3.25 to 400 μM).
Results: Flow cytometry analysis demonstrated the presence of positive expression of CD90 and CD44 in rBM-MSCs at passage 3, while the expression of CD34 and CD45 was found to be negative. Furthermore, our findings revealed that saffron at low concentrations, exhibited remarkable effects on the viability and growth promotion of rBM-MSCs. However, it should be noted that higher concentration of saffron were observed to exert cytotoxic effects.
Conclusion: Based on our research, it has been determined that saffron has the potential to augment the survival rate of MSCs and may be considered as supplementary therapeutic approach individuals undergoing MSC transplantation.
Keywords: Saffron, Bone Marrow-Derived Mesenchymal Stem Cells, Cytotoxicity, Cell Therapy

Ps-91: Musashi-2, A Knock-Out Target for Controlling The Malignancy of Melanoma Cells

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Objective: Musashi-2 (MSI2) is a novel oncoprotein that promotes cancer cell growth and invasion. Studies have shown that the expression of MSI2 increases in many types of cancers, such as cervical, kidney, papillary, and lung cancers. Melanoma is the most deadly form of skin cancer, often appearing as a dark spot on the skin. Metastasis occurs when melanoma cells spread through the skin lymph nodes, leading to skin lesions between the primary tumor site and the lymph region. The aim of this study is to investigate the potential oncogenic role of the MSI2 gene in melanoma cancer as a prognostic and/or therapeutic target. To achieve this, the MSI2 gene was knocked out in a melanoma cell line using the CRISPR/Cas9 technique to examine its impact on growth, proliferation, and invasiveness compared to unmodified cancer cells in the control group.
Materials and Methods: Initially, the expression level of *MSI2* was measured in two melanoma cell lines, A2058 and A375, using RT-qPCR. The cell line with the highest *MSI2* expression was chosen for further investigation. Two sgRNAs were selected to target the *MSI2* oncogene using bioinformatics and were then cloned into the pX459 plasmid. The melanoma cells were transfected with the Cas9 vector, and puromycin-resistant clones were isolated. Subsequently, the selected clones were analyzed to identify InDels in the genomic sequence of the *MSI2* gene through genomic polymerase chain reaction (PCR) and sequencing.
Results: The RT-qPCR results revealed a significantly higher expression level of *MSI2* in both melanoma cancer cell lines compared to healthy cells, with A2058 exhibiting the highest *MSI2* expression. Consequently, A2058 cells were selected for further investigation. On the other hand, the accuracy of the cloned sgRNA sequences was validated through PCR, enzymatic digestion, and sequence analysis. Following the transfection of A2058 cells with pX459 using Lipofectamine 2000 and the isolation of resistant clones, genomic DNA samples were extracted for genomic PCR.
Conclusion: Our findings confirmed biallelic deletions in the *MSI2* gene sequence between the two sgRNAs in the tested clones, resulting in a notable decrease in the proliferation rate of the cancer cells.
Keywords: Musashi-2, CRISPR/Cas9, Melanoma

Ps-92: Formulation, Physicochemical and Biological Characterization of Etoposide-Loaded Microemulsion

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Objective: Etoposide (ETO), an anticancer chemotherapeutic agent, is used in treatment of many types of malignancies. However, its low solubility restricts its use in clinical practice where in today's medicine it is tried to apply nano encapsulation to overcome its medical limitation. As an alternative, Microemulsion (ME) system as a nanoparticle drug delivery has been developed to improve ETO solubility and increase its delivery to malignant tissues. Therefore, in this study a newly developed ME system containing ETO was used to evaluate the physicochemical and its growth inhibition property against the MDA-MB-231 cancer cell line.
Materials and Methods: The ME drug delivery system has been prepared by phase titration method. Particle size and zeta potential were evaluated using dynamic light scattering (DLS), and drug release rate from the system was investigated *in vitro*. Safety of the DDS and its gradient was checked using bone marrow mesenchymal stem cells (BMSCs) and red blood cells (RBC). MDA-MB-231 cell line was used to check the DDS+ DXR and CXR only.
Results: The particle size was reported to be approximately 5.43 nm and its poly dispersity index (PDI) was 0.163. It was observed that the system and its components are safe. In addition, the drug loading rate was 92% and the releasing percentage of the drug after 24 hours through mouse skin and dialysis membrane was obtained as 49 and 62 %, respectively. The half maximal inhibition concentration (IC_{50}) of the drug for 48 and 72 hours of treatment was calculated to be 33.26 and 31.49 µg/ml respectively.
Conclusion: Newly developed ME shown to have high capacity to carry ETO its acceptable releasing rate which makes it a suitable carrier for this chemotherapeutic agent.
Keywords: Etoposide, Microemulsion, Breast Cancer, Drug Delivery

Ps-93: GATA1's Regulatory Network In Embryonic Stem-Like Cells: Bridging Spermatogonial Stem Cells To Pluripotency

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Objective: Embryonic stem-like cells (ES-like cells) offer promising potential in regenerative medicine since they can differentiate into any cell type, providing therapeutic potential for various disorders and injuries. Generating these cells from spermatogonial stem cells (SSCs) *in vitro* has gained attention as it involves a non-controversial, ethical source of pluripotent cells, bypassing the moral issues associated with embryonic stem cells. This method supports personalized medicine by using SSCs from an individual's tissue, reducing immune rejection risks and advancing reproductive health. The *GATA1* gene balances self-renewal and differentiation in embryonic stem cells by modulating gene expression networks. In pluripotent stem cells, *GATA1* is involved in the JAK/STAT, MAPK/ERK, and BMP signaling pathways.
Materials and Methods: We employed Fluidigm qPCR and immunocytochemistry staining to assess *GATA1* gene expression and protein levels in both cell types. Furthermore, we examined the expression of the Oct4 gene, a well-validated marker known to be up-regulated in pluripotent stem cells, to provide a comparative baseline for our data. We conducted protein-protein interaction (PPI) network analysis to enhance our study to iden-

tify proteins connected to the *GATA1* gene.
Results: Our analysis revealed significant fold changes in gene expression levels between SSCs and ES-like cells. Based on our data, the GATA1 gene is up-regulated in ES-like cells derived from SSCs. Immunocytochemistry analysis demonstrated presence of GATA1 protein within ES-like pluripotent stem cells. The PPI network analysis indicated a close relationship between *GATA1* and several key genes, including *TAL1*, *TCF3*, *RUNX1*, *LMO2*, and *LDB2*. We applied enrichment analysis based on gene ontology (GO) molecular functions. GO analysis highlighted the involvement of the GATA1 PPI network in transcription co-regulator binding, transcription co-regulator activity, and DNA binding.
Conclusion: The *GATA1* gene is assumed to exert a remarkable effect on the differentiation and function of ES-like cells derived from SSCs. We demonstrated that *GATA1* is significantly upregulated in ES-like cells and interacts with key genes involved in pluripotency and differentiation. These findings have promising implications for regenerative medicine, presenting a non-controversial, patient-specific source of pluripotent cells for disease treatment and fertility restoration.
Keywords: GATA1, Stem Cell, Regenerative Medicine, Embryonic Stem-Like Cells, Spermatogonial Stem Cells

Ps-94: A New Bioequivalent Based on Extracellular Vesicles and Spheroids for Wound Healing

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Objective: Non-healing wounds are common complications in patients with diabetes and venous insufficiency, leading to significant financial costs and a decreased quality of life. A combined bioink, consisting of hydrogel, cell spheroids, and extracellular vesicles, is being considered as a promising solution. In this system, the hydrogel provides support, while the spheroids form the basis of the construct. Our study focused on two types of extracellular vesicles - exosomes and matrix-bound vesicles (MBV) from mesenchymal stem cells as a potential agents for bioequivalent maturation.
Materials and Methods: For our study, we chose a hydrogel based on fibrin and gelatin due to its well-studied nature and optimal properties for bioprinting. We developed a protocol for creating a combined bioink and demonstrated that fluorescently labeled exosomes are absorbed by cells without negatively affecting the viability of spheroids in the hydrogel.
Results: We then optimized the standard protocol for MBV isolation. Through proteomic comparison of exosomes and MBVs, we found that exosomes have a richer proteomic profile than MBVs and contain more proteins responsible for construct maturation, particularly vascularization. *In vitro* experiments indicated that exosomes contributed to the formation of a more branched and longer network of tubules from MSC spheroids encapsulated in hydrogel, indirectly suggesting construct maturation. Based on *in vivo* experiments, we demonstrated that pure hydrogel, as well as hydrogel with MSC spheroids, when subcutaneously implanted in mice, did not trigger an immune response and integrated well into surrounding tissues.
Conclusion: This study represents the initial step towards creating combined constructs for treating non-healing wounds and generally open new approaches to the generation of combined bioequivalents. The study was financially supported by the Russian Science Foundation № 22-75-10120.
Keywords: Bioink, Hydrogel system, Extracellular Vesicles, Non-Healing Wounds,

Ps-95: A study of The Interesting Relationship between Differential Gene Expressions in Ovarian and Testicular Cancer

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Objective: Ovarian cancer is one of the most fatal gynecologic malignancies worldwide, with an estimated incidence of 239,000 cases and 152,000 deaths each year. Ovarian cancer and testicular cancer are distinct types of cancer with unique genetic landscapes and differential gene expression patterns.
Materials and Methods: We analyzed data from GO datasets (GSE172159, GSE17586, GSE15220, and GSE12630). Differentially expressed genes were studied in the limma package in the R language and TAC software. Enrichr carried out gene ontology, gene set enrichment, and genomic pathway analysis. Gephi, Cytoscape, and STRING databases were employed to build the network of protein-protein interactions.
Results: Ovarian cancer is characterized by genetic mutations in genes such as *BRCA1/2*, TP53, and *PIK3CA*, which drive cell proliferation, survival, and metastasis. In contrast, testicular cancer often involves mutations in genes like *KIT*, *KRAS*, and abnormalities in chromosomal structure, impacting cell growth and differentiation. Despite these differences, both cancers exhibit dysregulation of common pathways, including PI3K/AKT/mTOR signaling and DNA repair mechanisms, contributing to tumor development. Differential gene expression analyses reveal specific genes that are upregulated or downregulated in each cancer type, influencing cell cycle control, DNA repair, and stem cell-like properties.
Conclusion: Understanding these genetic differences is crucial for developing targeted therapies and identifying potential biomarkers for improved diagnosis and treatment outcomes in ovarian and testicular cancers.
Keywords: Ovarian Cancer, Testicular Cancer, Gene Expression, Signaling Pathway, Biomarkers

Ps-96: Safety of Autologous Exosomes Injection in Infertile Patients

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Objective: Some new researches have focused on mesenchymal stem cells (MSCs) as an option to ovarian regeneration. MSCs exert their effect by secreting exosomes in a paracrine manner. Evidence has shown that exosomes secreted from MSCs have

the same effect as MSCs. Given the role of exosomes in the improvement of ovarian function in animal models, this study investigated the safety and feasibility of autologous exosomes derived from menstrual blood MSCs injection into the ovaries of diminished ovarian reserve (DOR) patients.
Materials and Methods: In the first step, autologous MSCs were isolated from the menstrual blood of patients. Then, from the culture medium of the cultured cells, exosomes were isolated (using chromatography technique) and characterized (using flow cytometry, transmission electron microscopy, and dynamic light scattering). We tested the feasibility of intraovarian injection of autologous exosomes in the follicular phase in 10 DOR patients. The patients were aged 25-42 years without chronic malignancies. To assess the safety, some clinical symptoms such as fever, pain, infection, bleeding and allergic reactions were monitored for three months after the injection.
Results: The isolated exosomes had cup-shaped morphology. Their size was between 30-150 nm. Also, the expression of exosomal markers (CD9, CD63, and CD81) was positive for these vesicles. After the injection, the patients were discharged from hospital without pain, nausea, bleeding or fever. However, two patients experienced pain in the injection area. This pain lasted for 24 hours. Then it decreased and disappeared completely after 48 hours. In addition, there were no suspicious symptoms such as swelling, fluid collection, infection, or fever on physical examination or ultrasound during follow-up.
Conclusion: Due to the absence of serious side effects after injection, autologous exosomes derived from menstrual blood MSCs can be considered as a promising candidate for ovarian disorders after more extensive studies on efficacy.
Keywords: Diminished Ovarian Reserve, Exosomes, Mesenchymal Stem Cells, Regeneration Medicine, Clinical Applications

Ps-97: Different Artificial Antigen Presenting Cells in T Cell and Natural Killer Cell Expansion and Activation

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Objective: Artificial antigen-presenting cells (aAPCs) represent a promising technological advancement in immunotherapy, particularly for the expansion and activation of T cells and natural killer (NK) cells. These synthetic constructs mimic natural antigen-presenting cells (APCs) by presenting specific antigens in conjunction with necessary co-stimulatory signals and cytokines to immune cells, thereby facilitating their proliferation and functional maturation. Cytokines play a crucial role in immune cells. The development of aAPCs involves the integration of various biomaterials, bioengineering techniques, and cytokines to create platforms that can precisely control the presentation of antigens and co-stimulatory molecules. Recent studies have demonstrated the efficacy of aAPCs in expanding specific T cell and NK cell populations *ex vivo*, which can then be reintroduced into patients to target cancers, viral infections, and autoimmune disorders. Incorporating cytokines such as interleukin-2 (IL-2), interleukin-15 (IL-15), and interleukin-21 (IL-21) into aAPCs has been shown to enhance the proliferation and cytotoxic function of T cells and NK cells.
Materials and Methods: Various cell types can serve as the backbone for artificial antigen-presenting cells (aAPCs) each offering unique advantages for specific applications. K562 Cell Line, CHO (Chinese Hamster Ovary) Cells, HEK293 Cells, Jurkat T Cells, and Fibroblast Cell Lines are some backbones that have been used more. Each of these cell types has distinct characteristics that can be leveraged depending on the specific requirements of the immunotherapy being developed. We have chosen K562 and characterized the cell line by STR test and flow cytometry using specific antibodies.
Results: The report of the STR test demonstrated that our cell line(K562) has 16 markers matched with the STR profiling of the ATCC website. One marker had a different number of repetitions so flow cytometry data could cover this issue. The specific markers of APC had high expression on the K562 cell surface.
Conclusion: Choosing the best backbone to be aAPC is one of the challenges that has an important role in presenting antigens based on their use.
Keywords: Artificial Antigen-Presenting Cells, T Cell, NK Cell, Cytokines, K562 Cell Line

Ps-98: Investigating Foreign Body Response of Taurine Modified Transplantation Device for Type 1 Diabetes Cell Therapy

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Objective: Encapsulation devices for insulin-producing cells represent an advanced approach to treatment of type 1 diabetes (T1D). One of the major challenges in this approach foreign body response (FBR) of transplanted device. The FBR is the reaction of host immune cells to any implanted biomaterials and devices followed by transplantation preventing the diffusion of oxygen and nutrients in the device, leading to cell death. Despite attempts for reducing biomaterials fibrosis, development of cell therapy devices with low FBR remains challenge.
Materials and Methods: In this research, we design and fabricate a 3D-printed biocompatible device made of polylactic acid (PLA) and implanted subcutaneously on the dorsal side of mice. Surface modification of the device with taurine was performed to reduce FBR. Taurine, an anti-fouling and anti-inflammatory molecules, has been coated on the device surface in two methods including: physical coating, and covalent conjugation. Surface modification was confirmed by SEM-EDX, contact angle and colorimetry. *In vitro* anti-fouling properties were examined by measuring the amount of absorbed protein and macrophage adhesion on the surfaces. The gene expression of inflammatory markers was also investigated. Finally, the devices were implanted in mice for four weeks and retrieved for histological analysis.
Results: The SEM-EDX analysis revealed the distribution of taurine on the device surfaces, and the amount of the taurine coating was quantified using a colorimetric assay. The contact angle measurements of the modified surfaces indicated increased

hydrophilicity compared to the control group. Moreover, taurine effectively reduced protein fouling of the human serum albumin. The number of attached macrophages on taurine coating was significantly less than in the control group.
Conclusion: Our finding suggests that surface modification of devices with taurine coating can significantly reduce FBR *in vitro* model. This device showed a therapeutic potential approach for treatment of T1D.
Keywords: Type 1 Diabetes, Encapsulation, Foreign Body Response, Fibrosis, Taurine

Ps-99: Expression of miR-17-5p, SMAD6 and SMAD4 on *In Vitro* Cardiogenic Differentiation of Human Endometrium-Derived Stem Cells

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Objective: Myocardial infarction (MI) is the most common cause of heart failure and mortality worldwide. Due to the limited regeneration capacity of myocardium tissue, stem cell therapy is considered as a promising strategy to restore cardiac function. In this regard, molecular mechanisms involved in cardiogenic differentiation of MSCs, in particular the regulation mechanisms mediated by miRNAs and BMP–Smad signaling components remains elusive. In this study, we investigated the expression level of has-miR-17-5p, Smad4 and Smad6 Proteins in cardiac cells derived from human endometrium-derived mesenchymal stem cells (hEMSCs).
Materials and Methods: hEMSCs were primed with a cardiac-inducing medium containing 5-azacytidine and bFGF for a period of 24days. Smad6 and Smad4 proteins level, as well as the expression level of miR-17-5p were evaluated by immunofluorescence staining and qRT-PCR, respectively every 6 days.
Results: Immunofluorescence staining of Smad proteins indicated that upon cardiogenic differentiation of hEMSCs, the amount of Smad4 was significantly upgraded, while the expression levels of miR-17-5p and Smad6 during the induction period showed a completely oscillating differentiation. The Pearson correlation coefficients analysis revealed that there is a negative correlation between the Smad-6 with miR-17-5p.
Conclusion: Our results indicate that miRNAs-17-5p is involved in the cardiac differentiation of hEMSCs potentially by regulation of Smad6 levels through inhibitory effect. Although, more mechanistic experiments are required to confirmation of this idea.
Keywords: Endometrium-Derived Mesenchymal Stem Cells, Cardiomyocyte, Smad4, Smad6, Hsa-mir-17-5p

Ps-100: Predicting The Probability of Effectiveness of Terpenoid In The Treatment of Type 2 Diabetes Using in Silico Methods

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Objective: Type 2 diabetes is caused by the destruction of pancreatic β cells or insulin resistance in fat cells, liver, muscle, etc. Studies have shown that tumor necrosis factor (TNF-α) and Interleukin 6 (IL-6) among other cytokines, are two effective factors in the development of diabetes. so we are looking for them in this research by using in silico methods among terpenoids (plant compounds that have been seen to be useful in controlling diabetes) more favorable terpenoids be introduced and presented for further research.
Materials and Methods: Based on this, 1100 terpenoid structures along with all absorption, distribution, metabolism, excretion (ADME) properties were obtained from the website http://pscdb.appsbio.utalca.cl/ and after passing the screening process using the ADME properties and drug-likeness feature. Some of the ADME predictions included gastrointestinal absorption by BOILED-Egg method, interactions with Cytochrome P450 (CYP450) enzyme and being P-glycoprotein (P-gp) substrate. Drug-likeness is determined by Lipinski's "Rule of 5". These compounds were docked with TNF-α, IL-6 using Auto Dock Vina software .
Results: Using the screening methods, we reached 274 compounds that 4 compounds had good binding energy with both cytokines. These 4 compounds are Androstenedione, Testosterone, Limonin, Strigol, whose binding energy to TNF-α and IL-6 were -7.4 and -7.1, -7.1 and -6.9, -7 and -6.5, -7 and -6.4 respectively.
Conclusion: It seems that these 4 compounds (Androstenedione, Testosterone, Limonin, Strigol) that have been screened from 1100 terpenoids can moderate the effects of diabetes by simultaneously inhibiting TNF-α and IL-6 with their favorable binding energy.
Keywords: Type 2 Diabetes, Terpenoid, TNF-α, IL-6, In Silico

Ps-101: The Comparing Atudy among Various Human Mesenchymal Stromal Cell-Extra Vesicles on Mouse Retinal Ganglion Cells Injury

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Objective: Extracellular vehicles (EVs) derived from various mesenchymal stromal cells (MSCs) show significant potential for protecting retinal ganglion cells (RGCs). This study aims to identify the most effective EVs from the optimal MSC source for nerve regeneration.
Materials and Methods: EVs from various sources, including clonal bone marrow (cBM), dental pulp (DP), and trabecular meshwork (TM) MSCs isolated using different centrifugation methods, were tested in a mouse model with optic nerve crush injury. Following treatment, functional assessments, immunostaining, retrograde tracing of RGCs, and western blot analysis were used to evaluate recovery and identify superior EVs.
Results: These findings suggest that all four types of administered MSC-EVs improved the optomotor response. However, EVs derived from TM exhibited a lower survival rate for Brn3a+ RGCs. Due to the compliance with GMP standards of clonal MSC-EVs, we proceeded with these EVs. When comparing the cBM EVs to the control group, retrograde tracing of RGCs and visual behavior tests indicated that the results were more in line with those of an intact group. The 20K cBM EVs were found to upregulate the p-AKT/AKT and p-PI3K/PI3K ratios in the retina and optic nerve, which are known antiapoptotic indicators. In addition, vehicle was shown to quickly increase procaspase and caspase levels in the control group, whereas these apoptotic markers were reduced in retinas treated with EVs. Lastly, a comparative analysis of specific candidate proteins in the 20K and 110K cBM EVs revealed a higher concentration of TGFβ, a finding that was substantiated by western blot analysis of the retinal tissue.
Conclusion: Increased levels of AKT and PI3K through cBM EV 20K may be responsible for the degenerating RGCs protection afforded by multi-trophic factor within EVs. This discovery represents a significant advancement towards potentially employing cBM EVs in the healing of injured optic nerves.
Keywords: Optic Nerve Injury, Mesenchymal Stromal Cell, Extracellular Vesicle, Retinal Ganglion Cells, PI3 Kinase

Ps-102: Neural Differentiation of Mesenchymal Stem Cells Derived From Adipose Tissue On A Scaffold Prepared With A 3D Printer Using Exosomes Extracted From Neural Stem Cells

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Objective: Neural stem cell-derived exosomes (NSC-exosomes) are extracellular vesicles secreted by Neural Stem Cells (NSCs) that play essential roles in intercellular communication within the central nervous system (CNS). These exosomes are small membrane-bound vesicles containing various bioactive molecules such as proteins, lipids, and nucleic acids, which enable them to exert diverse therapeutic effects on neural cells and tissues. NSC-exosomes have been extensively studied for their potential therapeutic applications due to their ability to modulate cellular functions, promote tissue regeneration, and enhance neuroprotection. Several studies have demonstrated that these exosomes can transfer genetic information, including microRNAs and mRNAs, to target cells, leading to changes in gene expression and cellular behavior. One compelling feature of NSC-exosomes is their ability to promote neural cell proliferation and differentiation. These exosomes carry growth factors, transcription factors, and other signaling molecules that can induce the proliferation and differentiation of neural progenitor cells, thereby potentially aiding in the generation of new neurons and glial cells. This regenerative potential makes NSC-exosomes attractive candidates for therapeutic approaches to repair damaged neural tissue in neurodegenerative diseases or after neural injury.
Materials and Methods: First, nerve cell isolation, exosome isolation, scaffold construction, and then cell differentiation and the method of examining the differentiation of exosomes using ultracentrifuge method from neural stem cells extracted from mouse brain and identified by TEM microscope, western blot and DLS technique. Also, adipose stem cells placed on the 3D PAN scaffold were treated with exosome concentration for 14 days. Cell survival on the scaffold was evaluated by MTT and acridine orange ethidium bromide methods. Cell differentiation process was also investigated by immunocytochemistry and Real Time-PCR techniques. Examining the identity of exosomes confirmed the existence of exosomes with an approximate size of 70 nm. The results of cell survival indicate the ability of cells to survive and multiply within 14 days. Also, the expression of MAP2 (protein associated with microtubules) and Nestin (interstitial filament protein) was confirmed using immunocytochemistry method.
Results: Results (DLS diameter 49.79 nm), TEM (lipid bilayer membrane), expression of CD81, CD9 and CD63 markers and total protein concentration (160 µg/ml) identified exosomes. Immunophenotype of adipose mesenchymal stem cells (AdMSCs) was positive for CD73, CD90, CD105 markers and negative for CD34, CD45 markers. Morphological examination showed the transformation of AdMSCs towards neural differentiation from the fifth day under exosome treatment compared to the untreated group. The results of the expression of Nestin, Map2, Tuj-1 and NF markers in these two groups indicated a significant expression of neural differentiation of adipose mesenchymal stem cells located on the scaffold on the fourteenth day after treatment.
Conclusion: These results show that the use of NSC-exosomes can cause neural differentiation of adipose mesenchymal stem cells. Therefore, exosomes can be considered as a repair tool for the regeneration of the lost nerve tissue.
Keywords: Exosome, Adipose Mesenchymal Stem Cell, Neural Differentiation, 3D Printer

Ps-103: Neural Differentiation of Mesenchymal Stem Cells Derived from Adipose Tissue on A Scaffold Prepared with A 3D Printer Using Exosomes Extracted from Neural Stem Cells

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Objective: Neural stem cell-derived exosomes (NSC-exosomes) are extracellular vesicles secreted by neural stem cells (NSCs) that play essential roles in intercellular communication within the Central Nervous System (CNS). NSC-exosomes have been extensively studied for their potential therapeutic applications due to their ability to modulate cellular functions, promote tissue regeneration, and enhance neuroprotection. Several studies have demonstrated that these exosomes can transfer genetic information, including microRNAs and mRNAs, to target cells, leading to changes in gene expression and cellular behavior. One compelling feature of NSC-exosomes is their ability to promote neural cell proliferation and differentiation. These exosomes carry growth factors, transcription factors, and other signaling molecules that can induce the proliferation and differentiation of neural progenitor cells, thereby potentially aiding in the generation of new neurons and glial cells. The purpose of this project is to investigate the potential of inducing neural differentiation of these exosomes on adipose-derived mesenchymal stem cells (ADMSCs) in cultured conditions using a scaffold made with a 3D printer.
Materials and Methods: First, nerve cell isolation, exosome isolation, scaffold construction, and cell differentiation were conducted. The exosomes were extracted using the Anacell kit from neural stem cells and identified through TEM microscope, western blot, and DLS technique. Additionally, ADMSCs placed on the 3D PAN scaffold were treated with 100 µg/ml exosome concentration for 14 days. Cell survival on the scaffold was evaluated using MTT and acridine orange ethidium bromide methods. The cell differentiation process was further investigated using immunocytochemistry and Real Time-PCR techniques
Results: The results (DLS diameter 40.19 nm), TEM (lipid bilayer membrane), expression of CD81, CD9, and CD63 markers, and total protein concentration (160 µg/ml) identified exosomes. The immunophenotype of ADMSCs was positive for CD73, CD90, CD105 markers and negative for CD34, CD45 markers. Morphological examination showed the transformation of ADMSCs towards neural differentiation from the fifth day under exosome treatment compared to the untreated group. The results of the expression of Nestin, Map2, Tuj-1, and NF markers in these two groups indicated a significant expression of neural differentiation of adipose mesenchymal stem cells located on the scaffold on the fourteenth day after treatment.
Conclusion: These results demonstrate that the use of NSC-exosomes can induce neural differentiation of adipose mesenchymal stem cells. Therefore, exosomes can be considered a reparative tool for regenerating lost nerve tissue.
Keywords: Neural Differentiation, 3D Printer, Exosomes, Stem Cells

Ps-104: Identification of Potential Biomarkers with Breast Cancer Based on Bioinformatics Analysis

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Objective: Breast cancer is the most common malignancy in women worldwide, despite great advances in the diagnosis and treatment of cancer. Nowadays, with the advances in the bioinformatics analysis of RNAseq, it can identify potential biomarkers for diagnosis, treatment, and evaluation of metastasis and relapse. In this study, we are going to evaluate RNAseq data obtained from TCGA in breast cancer (BRCA) and investigate prognostic and protective genes in survival.
Materials and Methods: GEPIA2 (http://gepia2.cancer-pku.cn/) was used to examine the TCGA BRCA dataset in order to identify all DEGs linked with BRCA among high throughput RNA-Seq data. GEPIA2 is an online program that uses the genotype-tissue expression projects and the TCGA database to evaluate the transcriptional patterns of human malignancies and normal tissues. Genes with adj-P-value < 0.05 were considered significant; after that, significant genes were divided into 4 groups including up/down prognostic or protective genes according to the logFC and HR. After that, a Protein-protein interaction (PPI) network of significant genes associated with BRCA was constructed with STRING at the Cytoscape software.
Results: Of 3556 genes acquired from TCGA-RNAseq for AML, 334 genes are considered significant; of which 127 genes are prognostic and 207 genes are protective. PPI networks were drawn for significant and also hub genes; according to the result, 7 genes are considered as hub genes based on their interaction and degree including CXCL1, SELL, CXCL9, CD3E, CCL5, CXCR3, and CCR5 (degree more than 20). All genes were protective (adj P<0.05, HR <1).
Conclusion: This study identifies hub genes as a promising prognostic, protective, and diagnostic biomarker for breast cancer. Further investigations are warranted to identify the diagnostic potential of these genes.
Keywords: Breast Cancer, TCGA, RNAseq, Bioinformatics, Significant Genes

Ps-105: Understanding Specific Potential Genes for Acute Myeloid Leukemia by Pan-Cancer Analysis

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Objective: Acute myeloid leukemia (AML) is caused by functionally complementary genetic mutations that cause uncontrolled proliferation and maturational arrest of myeloid precursor cells. Nowadays, gene expression profile analysis is a potent research technique that reveals patients' dysregulated genes by integrating data from functional genomics, molecular transcription, and genetics. In this study, we are going to evaluate TCGA datasets in acute myeloid leukemia and investigate genes that are exclusively related to this cancer with pan-cancer analysis.
Materials and Methods: First, GEPIA2 was used to examine the AML dataset to identify all DEGs linked. Genes with a P<0.05 were considered significant; after that, significant genes were divided into 4 groups including up/down prognostic or protective genes according to the logFC and HR. A Protein-protein interaction network of significant genes associated with AML was constructed with STRING at the Cytoscape software, and hub-genes were identified based on their scores and interaction. In the end, we used Pan-cancer analysis with GEPIA2 and UALCAN for hub genes and got to the 4 genes that were exclusive.
Results: Of 7965 genes acquired from TCGA-RNAseq for AML, 843 genes are considered significant (adjusted P<0.05), of which 666 genes are prognostic and 174 genes are protective.

According to the result, 8 genes are significantly related to survival including PSMG1, SLC37A1, FAM207A, GPS2, CSTB, CHAF1B, AKAP9, and ABCG1 (p-value and P<0.05). PPI networks were drawn for significant genes and also hub genes. All of the genes except HSPA5 were prognostic. After pan-cancer analysis, we found NDUFS8, MRPL12, MRPL2, and SOD1 which are expressed significantly less than usual (Compared with other cancers as well as with normal samples).
Conclusion: This study identifies 4 genes that are involved specifically in the occurrence and progression of AML. This information may hold promise as potential biomarkers and therapeutic targets.
Keywords: Acute Myeloid Leukemia, TCGA, RNAseq, Bioinformatics, Pan-Cancer Analysis

Ps-106: Identification of Potential Biomarkers Associated with Ovarian Cancer Using An Integrated Bioinformatics Analysis

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Objective: Ovarian Cancer (OC) is an extremely deadly gynecological cancer. women are often diagnosed at an advanced stage due to the lack of available biomarkers. This study aims to analyze the potential hub-genes associated with the survival of these patients.
Materials and Methods: At first, GEPIA2 was used to examine the TCGA OV dataset in order to identify all DEGs linked with OV among high throughput RNA-Seq data. GEPIA2 is an online program that uses the Genotype-Tissue Expression (GTEx) projects and the TCGA database. Thereafter, significant genes (p-value ≤ 0.05) were divided into 4 groups including up/down prognostic or protective genes according to the logFC and HR. Also, a Protein-Protein Interaction (PPI) network of significant genes associated with OV was constructed with STRING at the Cytoscape software for identifying hub-genes associated with OV cancer. Next, we used TISIDB to evaluate the immune system's interaction with hub-genes which play a major role in cancer onset, development, and treatment. Ultimately, enrichment analysis including Gene Ontology (GO) was used to explore the related biological processes, molecular function, cellular components, and Kegg pathway analysis.
Results: From 7638 genes obtained from TCGA-RNAseq for OV, 341 genes are prognostic and 241 are protective, divided into down and up categories. According to PPI networks, we identified 7 hub-genes based on their degree and interaction, including CXCR4, CXCL10, RPL23, CXCL9, UBD, GZMB, and TNFSF13B. Also, the result of TISIDB showed that most hub-genes have a strong interaction with the immune system except RPL23 and CXCR4 which have less interaction. Ultimately, the enrichment analysis showed these genes have the strongest significance in the inflammatory response, cytolytic granule, CXCR Chemokine Receptor Binding, Cytokine-cytokine receptor interaction, etc.
Conclusion: Our study identified 7 hub-genes that might be involved in the prognostic, diagnosis and survival of OV. Further investigations are warranted to identify the therapeutic potential of these genes.
Keywords: Bioinformatic Analysis, Ovarian Cancer, Biomarker

Ps-107: Mesenchymal Stromal Cell-Extracellular Vesicles-Loaded MiR-29a Induced Apoptosis in HCC Cell Lines

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Objective: In spite of significant advancements in therapeutic modalities for Hepatocellular Carcinoma (HCC), there is still a high annual mortality rate with a rising incidence. There are different treatment strategies that can induce apoptosis in cancer cells. MiRNAs (miRs) are short, 18-24 nucleotide-long molecules belonging to a class of highly conserved Non-Coding RNAs (ncRNAs) that regulate the expression of genes related to main cellular pathways post-transcriptionally. MiR-29a belongs to the miR-29 family and exerts anti-tumor impacts in diverse cancers including HCC. Since myriad biological processes are regulated by miRs, their pharmacological modulation has gained increasing interest as anticancer therapy. However, their effective delivery is hampered due to their negatively charged nature which affects their uptake into the cells. Extracellular Vesicles (EVs) encompass a wide range of vesicles originating from cells, among them endosome-derived exosomes, cell membrane-derived ectosomes, and apoptotic bodies released from dead cells. Mesenchymal stromal cells-derived EVs (MSCs-EVs) are particularly valued in drug delivery system in recent years. In the current study, we aimed to investigate the impact of treatment with miR-29a on the apoptosis in HCC cells using EVs as a natural delivery system given their potential in miRNA delivery both *in vitro* and *in vivo*.
Materials and Methods: Human Wharton's Jelly mesenchymal stromal cell-derived extracellular vesicles (WJ-MSC-EV20K) were lately isolated through centrifugation, characterized by Western blot, scanning electron microscopy, and dynamic light scattering. MiR-29a was subsequently loaded into the EVs and its loading efficiency was evaluated via RT-qPCR. Flow cytometry assessment was then performed on Huh-7 and HepG2 cell lines to evaluate apoptosis.
Results: Findings indicated that MSC-EVs can effectively delivered miR-29a to HCC cells. Furthermore, EV20K-miR-29a treatment significantly induced apoptosis in Huh-7 and HepG2 cells probably through the downregulation of anti-apoptotic gene MCL1.
Conclusion: Given the efficient delivery of miR-29a by EV20K, and the role of miR-29a ability in apoptosis induction in HCC cells, the use of EV20K-miR-29a could be a promising approach for liver cancer treatment.
Keywords: Hepatocellular Carcinoma, Apoptosis, MiR-29a, Extracellular Vesicles

Ps-108: *In Vitro* Differentiation of Adipose Derived Mesenchymal Stem Cells into Insulin-Producing Cells on Decellularized Peritoneal Scaffold

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Objective: Diabetes mellitus (DM) is a set of chronic metabolic diseases caused by insulin insufficiency. DM is highly prevalent, and its incidence is rising globally. At present, there are different treatments for diabetes. Recently, the differentiation of stem cells, especially Adipose-derived stem cells (ADSCs), and using natural scaffolds have demonstrated considerable promise as an alternate technique in the treatment of diabetes patients. Therefore, the aim of this study is to produce insulin-secreting cells from ADSCs using peritoneal scaffolds.
Materials and Methods: For this purpose, ADSCs were extracted from rat fat and differentiated during 2 stages using ITS and nicotine in 14 days. Scaffold formation and cell differentiation were evaluated using Masson's trichrome staining, Diamidino-2-Phenylindole (DAPI) staining, and western blotting.
Results: Histological analysis of Masson's trichrome-stained processed peritoneum samples shows complete decellularization with preservation of extracellular matrix microarchitecture. Further, staining of tissue samples with DAPI demonstrates the complete removal of DNA fragments. Western blot analysis also showed that the differentiation groups with peritoneal scaffold expressed beta cell-specific proteins such as MAFA and PDX1 significantly more than the control group ($P<0.0001$). Also, the 3D group demonstrated MAFA ($P<0.0001$) and PDX1 ($P<0.01$) protein expression significantly more than the 2D group.
Conclusion: These results collectively have evidenced that the decellularized peritoneum is a suitable scaffold for stabilizing artificial pancreatic islands. Peritoneum scaffold is thus capable of producing insulin-secreting cells from ADSC and could be widely applied as one of the differentiation agents.
Keywords: Adipose Tissue Derived Mesenchymal Stem Cells, Diabetes Mellitus, Decellularized Scaffold, Peritoneal Scaffolds, Insulin-Producing Cells

Ps-109: Overcoming Cisplatin Resistance in Ovarian Cancer: A Promising Approach with Quercetin-Loaded Solid Lipid Nanoparticles

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Objective: Ovarian cancer (OCa) is a significant health concern globally, with rising mortality rates despite it being less common in Iran compared to Western countries. The prevalence of epithelial carcinoma, the most common type of OCa, and the development of resistance to platinum-based chemotherapy, such as cisplatin, present major therapeutic challenges. This study aims to investigate the potential of quercetin (QU)-loaded solid lipid nanoparticles (SLN) to overcome cisplatin resistance in OCa cells.
Materials and Methods: Human ovarian cancer cell lines SKOV-3 was exposed to 36 µl/ml of QT-SLN or 0.001 µl/ml cisplatin for 48 hours. To assess the toxicity of QT-SLNs, cell viability and RT-PCR were measured. ovary cancer cell proliferation was investigated through MTT assay. Finally, the effect of treatments on gene expression of XIAP was evaluated by quantitative real-time PCR.
Results: We discovered thate quercetin facilateds cispelatin-induced apoptosis in human ovary (cell line SKOV-3) by inhibiting the anti-apoptotic protein XIAP. Following QT-SLNs treatment, the expression of the XIAP protein significantly decreased, while the XIAP expression showed some change in comparison with free QT-treated cells. when cancer cells are pretreated with nano-quercetin.
Conclusion: The application of QT-SLN in conjunction with cisplatin not only diminishes cell proliferation and augments apoptosis but also effectively curtails the expression of genes associated with drug resistance. These findings suggest that QT-SLN could be a viable strategy to overcome cisplatin resistance, offering a promising therapeutic avenue for inclusion in clinical OCa treatment protocols.
Keywords: Solid Lipid Nanoparticles, Resistance, Cisplatin, Quercetin, Ovarian Cancer

Ps-110: Comparison of The Effects of Exosomes Secreted from Menstrual Blood-Derived Stem Cells and Ginger-Derived Exosomes on Apoptosis in Endometriosis Women

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Objective: The most important theory for endometriosis initiation is the return of blood during menstruation. Menstrual blood-derived stem cells from endometriosis patients (E-MenSCs) have shown different gene expression compared with healthy non-Endometriotic women's cells (NE-MenSCs). Today, exosomes extracted from mesenchymal stem cells and plants have been considered for the treatment of various diseases. In this study, we compared the effect of NE-MenSCs-derived exosomes and exosomes derived from the root of ginger on E-MenSCs.
Materials and Methods: Menstrual blood samples were collected from healthy and endometriosis women. MenSCs were isolated through Ficoll-Paque density gradient centrifugation and cultured till 3rd passage. After a gradual decrease of FBS

concentration in the culture medium, NE-MenSCs-derived exosomes (C-Exo) were isolated and characterized. In addition, plant exosomes (P-Exo) were extracted from the root of ginger. 72 hours after treating E-MenSCs with C-Exo/ P-Exo, cell viability was measured using apoptosis assay, and the expression of genes related to apoptosis was analyzed by Real-Time polymerase chain reaction (PCR).
Results: After treatment, increased apoptosis was observed in both P- and C-Exo groups compared to the untreated group of E-MenSCs. Also, the expression level of BAX/BCL2 in the P-Exo group was significantly decreased compared to the E-MenSCs group. Besides, the apoptosis level was decreased after P-Exo treatment compared to E-MenSCs.
Conclusion: Although the effect of exosomes, especially P-Exo, has been significant in this study, it seems that further studies on the wider range of treatment doses, as well as preclinical and clinical studies, are necessary for providing an effective treatment method for endometriosis.
Keywords: Endometriosis, Exosome, Mesenchymal Stem Cells, Menstrual Blood, Ginger

Ps-111: The Comparative Evaluation of The Effects of Small Molecule C-82 and Naringenin on The Inflammatory Factors of Menstrual Blood Derived-Stem Cells in Endometriosis Patients

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Objective: One of the leading causes of endometriosis - a chronic estrogen-dependent disease associated with pelvic pain and infertility- is the return of menstrual blood flow into the pelvic cavity and the establishment of menstrual blood mesenchymal stem cells (MenSCs) in areas outside the uterine cavity. Menscs from endometriosis patients (E-MenSCs) and healthy women have been shown to vary, particularly in terms of surface markers and gene expression, which may suggest the involvement of these cells in the development, expansion, and maintenance of ectopic lesions. The purpose of this study is to investigate the effect of small molecule C-82 and naringenin as inhibitors of involving pathways on E-MenSCs to modulate their gene expression and functional pattern.
Materials and Methods: Briefly, menstrual blood samples (2-3 ml) were collected from women with endometriosis. E-MenSCs isolated by Ficoll-Paque density-gradient centrifugation were characterized by flow cytometry. Then E-MenSCs cells were treated with small molecule C-82 and naringenin in the third passage, then the cell behavior of the studied groups was investigated using ELISA and Western methods.
Results: In this study, using the ELISA test, we found that naringenin and C-82 treatment can reduce the production level of ROS, IL-6, and IL-8 in the endometriosis cell line, moreover, when we compared the treated groups, showed that combined treatment with C-82 and Naringenin was more effective in reducing all three relevant genes in E-MenSCs. Also, using Western analysis, the expression level of the β-catenin gene and α-SMA protein showed a significant decrease in all treated groups compared to untreated E-MenSCs.
Conclusion: The results obtained from this study clarify the function of C-82 together with naringenin in modulating E-MenSCs. However, it seems that more research is needed to analyze the precise effects of small molecule C-82 and naringenin on endometriosis.
Keywords: Endometriosis, Menstrual Blood Derived-Stem Cells, Small Molecule C-82, Naringenin, Inflammatory Factors

Ps-112: Identification of Three Key microRNAs (miR-302d, miR-371, miR-372) Involved in The Cardiomyocytes' Cell Cycle Arrest

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Objective: Cardiomyocytes' cell cycle arrest is the major underlying mechanism for the limited cardiac regenerative capacity. As a result, myocardium is replaced with fibrotic tissue after ischemic or non-ischemic damage, which reduces the heart's blood pumping efficiency. In order to enhance the regenerative capacity, one solution could be the identification of the molecular basis of cardiomyocytes' cell cycle arrest. In the current study, we aimed to investigate miRNAs related to this cellular process.
Materials and Methods: Initially, we reanalyzed the RNA sequencing (RNA-Seq) data for differentiating human induced pluripotent stem cell-derived cardiomyocytes available in public dataset NCBI (GSE35672) using GEO2R with $-2 \geq LogFC \geq 2$ and adj.$P \leq 0.05$ with focus on miRNA expression profile. The Differentially Expressed miRNAs (DEmiRNAs) were identified and their corresponding signaling pathways were determined using Enrichr. In a further screen, those DEmiRNAs related to proliferation, growth and cell cycle were shortlisted. To verify these candidate DEmiRNAs, human embryonic stem cells (hESC, Royan H6 line) were expanded and differentiated into cardiomyocytes using four small molecules targeting Wnt/α-catenin, TGFα and sonic hedgehog pathways. Cardiomyocytes were harvested at day 10 (D10), D20 and D30 of differentiation and subjected to cell cycle analysis by flow cytometry. The expression of candidate DEmiRNAs were evaluated in hESC and cardiomyocytes at D10, D20 and D30 using real time qRT polymerase chain reaction (PCR).
Results: miR-302d, miR-371 and miR-372 were identified as the candidate DEmiRNAs, where miR-302d and miR-372 was related to Wnt/α-catenin, sonic hedgehog and cancer pathways and miR-371 to Wnt/α-catenin and cancer pathways. The cell cycle analysis showed that while $53.2 \pm 2.5\%$ of hESC were in G1, the percentage was significantly increased in D10, D20 and D30 cardiomyocytes (74, 77.4 and 80%, respectively). Conversely, the percentage of cells in S phase was significantly decreased in D10, D20 and D30 cardiomyocytes compared to hESC (13.1, 8.61 and 5% compared to 23.7%, respectively). miR-302d, miR-371 and miR-372 showed downregulation in hESC-derived cardiomyocytes at D20 and D30.
Conclusion: Thus, the decreased expression of candidate DEmiRNAs by increasing differentiation window, suggests them as potential molecular regulators of cardiomyocytes' cell cycle arrest and possible candidates for cell cycle reentry by overexpression.

Keywords: Human Pluripotent Stem Cell, Cardiac Differentiation, Regulatory Non-Coding RNA, Cell Cycle

Ps-113: Treatment with Cabergoline Reduced The Expression of Immune Checkpoints in Monocyte-Derived Dendritic Cells and Shifted Their Phenotype to Tolerogenic Dendritic Cells

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Objective: Dendritic cells (DCs) are regarded as specialist antigen-presenting cells, several strategies have been used recently to increase the effectiveness of antigen presentation, tolerogenisity and improving immune system against several disorders including autoimmune diseases. Tolerogenic dendritic cells inhibit autologous T-cell responses, making them appealing therapeutic candidates for autoimmune disorders.
Materials and Methods: We investigate the impact of cabergoline on the expression of immune checkpoints in dendritic cells generated from peripheral blood mononuclear cells. Ficoll was used to isolate PBMCs, while magnetic activated cell sorting was used to separate monocytes with high purity. DCs were generated from monocytes after cell were cultured in a special medium for 5 day and Apoptosis assay was done to determine the optimal dosage of cabergoline Using flow cytometry and Annexin v/Propidium iodide labeling. Finally, qRT-PCR assay was done for recognizing the tolerogenic profile of DCs and analyzing the level of immune checkpoint expression in DCs.
Results: The purity of isolated monocytes separated from PBMCs using MACS method was 92.5%. Administering 10 μM of cabergoline to the cells does not result in a significant loss of life. The both the mDC group and the treatment group with 10 μM drug doses, expressed CD11c, HLA-DR, and CD86 markers. Then, the mean fluorescence intensity showed the level of the cabergoline-treated group had a significant increase in CD11c and CD86 expression (p,0.05). While the decrease in HLA-DR expression was not significant in the Cabergoline-mDC group. The expression of the CTLA-4 genes (P≤0.01), B7H7 (P≤0.05) and ICOS-L (P≤0.0001) decreased significantly in Cabergoline-mDCs, and TIM-3 expression level had a significant elevated after cabergoline treatment (P≤0.01). however, PD-L1 and CD39 decrease was not significant.
Conclusion: Our findings demonstrated that cabergoline treatmented DCs could be effective in autoimmune diseases according to their remarkable role in reduction of immune checkpoints expression.
Keywords: Cell Therapy, Autoimmune Disease, Cabergoline, Immune Checkpoint Molecules, Dendritic Cell

Ps-114: Treatment with Cabergoline Reduced The Expression of Oncogenic Immune Checkpoints in Monocyte-Derived Dendritic Cells and Shifted Their Phenotype to Immunogenic Dendritic Cells

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Objective: Dendritic cells (DCs) regarded as specialist antigen-presenting cells. Strategies used recently to increase the effectiveness of antigen presentation, tolerogenic and generate strong immune response against disorders such as autoimmune disorders. Tolerogenic dendritic cells inhibit autologous T-cell responses, making them appealing therapeutic candidates for autoimmune diseases.
Materials and Methods: DCs were generated from monocytes after cell were cultured and Apoptosis assay was done to determine the optimal dosage of cabergoline Using flow cytometry and Annexin v/ iodide labeling. Administering 10 μM of cabergoline to the cells doesn't result in a significant loss of life. m DC group and the treatment group with 10 μM drug doses, expressed CD11c, HLA-DR, and CD86 markers. the mean fluorescence intensity showed the level of the cabergoline-treated group had a significant increase in CD11c and CD86 expression (p,0.05). While the decrease in HLA-DR expression was not significant in the Cabergoline-m DC group. qRT-PCR assay was done for the recognizing the tolerogenic profile of DCs and analyzing the level of immune checkpoint expression in DCs.
Results: Results indicated that the expression of the CTLA-4 genes (P≤0.01), B7H7 (P≤0,05) and ICOS-L (P≤0.0001) decreased significantly in Cabergoline-m DCs, and TIM-3 expression level had a significant elevated after cabergoline treatment (P≤0.01). PD-L1 and CD39 decrease was not significant.
Conclusion: Findings demonstrated that cabergoline treatment DCs could have an impressive effect in autoimmunotherapy according to their remarkable role in immune checkpoints expression.
Keywords: Cell Therapy, Autoimmune Disease, Cabergoline, Immune Checkpoint Molecules, Dendritic Cell

Ps-115: Diagnosis of Drug Resistance in Brain Tumor Patients Using Chemobiogram Kit

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Objective: The chemogram kit is an innovative method used in oncology to optimize the selection of chemotherapy drugs for cancer patients. Oncologists extract a sample from the patient's tumor. After tumor cells are cultured in the laboratory, the cells are exposed to a diverse panel of chemotherapy drugs. By evaluating the response of tumor cells to different drugs, specialists can identify the most effective treatments. This helps in the early detection of drug resistance
Materials and Methods: Initially, common chemotherapy drug doses used in adult human treatment were adapted from Medscape.com and converted to culture medium doses. Tumor cells from cancer patients were cultured in both 2D and 3D culture. Subsequently, tumor cells were exposed to chemotherapy drugs for 24, 48, and 72 hours. To assess cell viability, the MTS Assay was employed, and measurements were obtained using a Micro-

plate reader.
Results: The greatest effect of drugs on the glioblastoma cell line (U251) was for: % Viability 2% Viability 1 Group (24,72H 2D) 100 100 Control 1 69 68 Gemsiban 72H 2 18 20 Cisplatin 24H 3 17 20 Doxorubicin 24H 4 18 17 Bevacizumab 24H 5 % Viability2 % Viability1 Group (72H 3D) 100 100 Control 1 69 68 TMZ 72H 2.
Conclusion: The Chemobiogram Kit is a powerful tool used by oncologists to optimize chemotherapy drug selection for individual cancer patients.
Keywords: Brain Cancer, Glioblastoma, U-251G Cell Line, Drug Resistance, Drug Treatment

Ps-116: Selenium-Containing Polycaprolactone 3D-Printed Scaffold for Osteogenesis

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Objective: Bone injuries are a prevalent issue that affects millions of people worldwide. Selenium is an essential trace element that plays crucial roles in maintaining bone health due to antioxidant and anti-inflammatory properties. Selenium deficiency delays or disrupts bone healing. In the present study, with the approach of producing a simple and efficient implant containing the selenium, PCL scaffolds containing the selenium were produced using a 3D printer and its effect on bone repair was investigated in the *in vitro* conditions.
Materials and Methods: Net and selenium-containing (0.5-10 uM) PCL scaffolds were produced with 3D printer. Rat bone marrow mesenchymal stem cells were cultured on the scaffolds, and the osteo-induction potential of PCL-Sel scaffold was compared with net PCL scaffold during the bone differentiation of BMSCs. The biocompatibility of 3D-printed scaffolds was assayed using MTT assay.
Results: The study's findings revealed that incorporating selenium to PCL enhanced the scaffold's hydrophilicity. In addition, selenium had a gradual release from the scaffolds and Bone differentiation of cells on PCL-selenium scaffolds was higher compared to pure PCL. The MTT test results showed that PCL scaffolds incorporated with 0.5-10 µM selenium had not toxic effect on the BMSCs and did not inhibit their growth.
Conclusion: The results of the current study demonstrated that selenium-incorporated PCL scaffold had improved bone adaptability and osteogenesis capacity because of selenium's favorable bone-formation capabilities and might be used to treat bone defects.
Keywords: Polycaprolactone, 3D-Printed Scaffold, Selenium, Tissue Engineering

Ps-117: Bardoxolone Methyl Increases The Antioxidant Content of Bone Marrow Mesenchymal Stem Cell-Derived Exosomes

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Objective: Bone marrow mesenchymal stem cell (BMSC)-derived exosomes have been recognized as a promising therapeutic modality due to their low immunogenicity, and the ability to penetrate biological barriers. The cargo carried by exosomes is determined by the cells from which they originate. By inducing donor cells with specific small molecules before isolating exosomes, it would be feasible to generate exosomes that carry specific molecules, such as antioxidants. This research aimed to enhance the antioxidant capacity of exosomes by activating the nuclear factor Erythroid 2-Related Factor 2 (*NRF2*) gene in BMSCs.
Materials and Methods: BMSCs were harvested from Wistar rats and treated with Bardoxolone methyl (BaMet) to upregulate the *NRF-2* gene. Real-time polymerase chain reaction (PCR) was performed to determine the expression level of *Nrf2*. Exosomes were isolated by ultracentrifugation. Their identity was confirmed using DLS, SEM, TEM, and Western blot analyses to detect markers specific to exosomes. The antioxidant contents of exosomes were determined using Superoxide Dismutase (SOD) and catalase (CAT) assay kits.
Results: The BaMet-treated BMSC-derived exosomes exhibited spherical morphology with a mean size of 84.79 ± 10.79 nm. Immunoblotting revealed that the exosome tested positive for CD63, CD9, and CD81. BaMet-treated BMSC-derived exosomes exhibited significantly higher levels of SOD (2.890 ± 0.085 vs. 1.070 ± 0.071) and CAT content (0.333 ± 0.016 vs. 0.159 ± 0.008) ($P<0.05$).
Conclusion: Our findings demonstrated that the elevated expression of the *Nrf2* gene in BMSCs stimulated the secretion of exosomes with increased antioxidant content.
Keywords: Exosome, Mesenchymal Stem Cell, Antioxidant, NRF2

Ps-118: Synergistic Effects of Kartogenin and TAK242-Loaded Extracellular Vesicles in Treatment of Rheumatoid Arthritis

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Objective: Extracellular vesicle (EV)-based drug delivery systems show great promise for treating systemic inflammatory diseases like rheumatoid arthritis (RA). Unlike conventional anti-inflammatory agents, which often have non-specific tissue distribution and uncontrolled drug release, EV-based systems provide precise delivery and controlled release of therapy. This study specifically focused on EVs loaded with Kartogenin (KGN) to promote chondrogenesis and TAK-242 to reduce inflammation in a collagen-induced arthritis (CIA) rat model.
Materials and Methods: TAK242 and KGN were loaded into EVs using electroporation and sonication, respectively, and were characterized by SEM, DLS, and zeta potential analysis. For *in vivo* evaluations, animals were divided into five treatment

groups: EV TAK242, KGN, combined TAK242 and KGN, and EV/TAK242-KGN. Results were compared with sham, healthy, and methotrexate control groups. Over a 28-day post-treatment follow-up, physical examinations, imaging, histopathological, and molecular tests were conducted to evaluate treatment response and underlying biological mechanisms.
Results: TAK242 and KGN were efficiently loaded into EVs, with encapsulation efficiencies of 11.15 and 39.85%, respectively, while maintaining the general characteristics of EVs. Physical observations showed significant reductions in paw swelling and arthritis severity, along with increased body weight in the treatment groups. The EV/TAK242-KGN group exhibited the most notable improvements compared to the other groups. Radiographic and histological analyses confirmed the therapeutic effects of EV/TAK242-KGN in CIA rats. Additionally, there was a decrease in serum levels of the pro-inflammatory cytokines IL-6, IL-17, and TNF-α, and an increase in the anti-inflammatory cytokine IL-10 across all treatment groups compared to the sham group, with the most significant changes observed in the EV/TAK242-KGN group.
Conclusion: EV-based drug delivery systems, especially EVs loaded with KGN and TAK-242, offer a promising therapeutic strategy for RA treatment and could apply to targeted therapies for systemic conditions.
Keywords: Rheumatoid Arthritis, Extracellular Vesicles, Drug Delivery, TAK242, Kartogenin

Ps-119: Design and Fabrication of Conductive Hydrogel Based on Polyaniline/Sodium Alginate for Bone Tissue Engineering

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Objective: Bone tissue engineering aims to mimic the natural extracellular matrix (ECM) environment to promote osteogenesis and repair bone defects. The ECM in bone tissue is a dynamic and conductive network that supports cellular activities essential for bone regeneration. Sodium alginate (SA), a natural polysaccharide, is widely used for its biocompatibility and gel-forming properties, while Polyaniline (PANi) offers electrical conductivity, enhancing cell proliferation and differentiation. Incorporating drugs can enhance scaffold functionality by providing additional bioactive properties and supporting tissue regeneration.
Materials and Methods: Sodium alginate was dissolved in deionized water, followed by the addition of an appropriate drug amount. Aniline was then added to the mixture, and finally, ammonium persulfate (APS) was introduced to initiate the polymerization of aniline. This polymerization process led to the formation of a conductive SA/PANi hydrogel without the need for additional crosslinkers, as the polymerized aniline acted as the crosslinking agent. Various parameters, including polymer concentrations and polymerization conditions, were optimized to achieve the desired hydrogel. The composite hydrogel's properties were characterized using Fourier-Transform Infrared Spectroscopy (FTIR), Scanning Electron Microscopy (SEM), and conductivity tests.
Results: FTIR analysis revealed distinct spectral features confirming the successful polymerization of aniline and gelation of sodium alginate within the composite hydrogel scaffold. Additionally, shifts and broadening of peaks associated with sodium alginate indicated its structural rearrangement and hydrogen bonding interactions with the polymerized aniline. SEM images displayed a uniform and porous structure in the SA/PANi hydrogel scaffold. Conductivity tests confirmed the hydrogel's good electrical conductivity.
Conclusion: A conductive drug-loaded SA/PANi hydrogel scaffold was developed, presenting a promising candidate for bone tissue engineering.
Keywords: Bone Tissue Engineering, Alginate, Polyaniline, Conductive Hydrogel, Osteogenesis

Ps-120: Features of Electrspun Nanofibers Mounted on Each Other Containing Collagen-Based Hydrogel for Tissue Engineering Applications

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Objective: Electrospun nanofibers, which can mimic the nanostructure of an extracellular matrix within native tissue, have extensively been applied in tissue engineering-based approaches.
Materials and Methods: To do this experimental study, hybrid materials containing synthetic and natural polymers were electrospun and mounted on each other aimed at imitating the structure of native ECM and improving the aspects of applied materials (natural and synthetic polymer) in combination with each other and compatibility of fabricated constructs. Simultaneously, collagen-based hydrogels prepared in the HCL solution were loaded into the interface of these mounted nanofibers, followed by crosslinking in the EDC/NHS solution and freeze-drying. In addition, one construct containing the desired hydrogel without applying nanofibers was considered the control group. In the following, corresponding features, including cell compatibility, porosity, and *in vivo* study, were investigated.
Results: The SEM imaging revealed the fibrous structure of electrospun nanofibers and multilayered structures of fabricated constructs. In addition, it was revealed that the porosity of all multilayered constructs was ≥ 85%, and an HDF cell-seeded construct with two layers of nanofibers within its structure had the best cell interaction, confirmed by FESEM imaging. *In vivo* studies of subcutaneously implanted samples demonstrated lower inflammatory responses in constructs containing one and two layers of nanofibers compared to the control one.
Conclusion: Based on these results, it could be concluded that the electrospun nanofibers accompanied by collagen-based hydrogels could be the proper choice for simulating the native tissue structure and improving the compatibility of implanted constructs.

Keywords: Nanofiber, Electrospinning, Collagen- Based Hydrogel

Ps-121: Uterine Fluid Derived Exosomes Enhance Endometrial Receptivity by Upregulating Leukemia Inhibitory Factor and Downregulating Mucin-16 Genes in Endometrial Cells

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Objective: Endometrial exosomes carry bioactive agents to uterine epithelial cells and trophectoderm to promote implantation. This study investigates the probable molecular mechanisms by which exosomes improve endometrial receptivity.
Materials and Methods: Exosomes were isolated from uterine fluid by Gradient ultracentrifugation and characterized by dynamic light scattering (DLS), Transmission Electron Microscopy (TEM), and western blotting. Endometrial Ishikawa cell line were treated with isolated exosomes and *in vitro* implantation assay was performed to evaluate the effect of exosomes on the receptivity potential of endometrial cells. Finally, the expression of several endometrial receptivity markers was evaluated by Real-Time polymerase chain reaction (PCR).
Results: DLS graph and TEM imaging showed that the isolated exosomes had a cup-shaped or spherical morphology with a mean size of 91.8 nm and zeta potential of -9.75 mV. Relatively strong immunoblotting bands for exosome-specific protein markers (CD-9 and CD-81) confirmed the isolation of exosomes. *In vitro* implantation assay revealed that treatment of endometrial cells by uterine exosomes enhances the receptivity potential of endometrial cells 1.5 ± 0.5 folds relative to the control group. Gene expression analysis showed that treatment of endometrial cells with uterine-derived exosomes results in upregulation and downregulation of Leukemia Inhibitory Factor (LIF) and Mucin-16, respectively; however, the expression of Trophinin and Insulin-Like Growth Factor-Binding Protein 1 (IGFBP1) was not affected.
Conclusion: These findings confirmed the vital role of exosomes in endometrial receptivity and showed that regulation of LIF and Mucin-16 expression is one of the probable mechanisms by which exosomes affect endometrial receptivity.
Keywords: Exosomes, Endometrium, Receptivity

Ps-122: An Injectable Type II Collagen/Hyaluronic Acid Hybrid Hydrogel A Step Towards An Extracellular Matrix-Inspired Scaffold for Cartilage Regeneration

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Objective: The extracellular matrix (ECM) plays a vital role in regulating cellular functionality and tissue regeneration, providing both compositional and architectural cues. In this study, Type II collagen (COL-II) and hyaluronic acid (HA), as the main components of cartilage, were grafted with tyramine (HA-Ty and COL-II-Tyr) to design an injectable bioinspired hydrogel scaffold for cartilage regeneration.
Materials and Methods: COL-II was purified from chicken sternums, and COL-II-Tyr and HA-Tyr conjugates were synthesized. The conjugates were crosslinked in the presence of horseradish peroxidase enzyme (HRP) and a cytocompatible concentration of Hydrogen Peroxide (H_2O_2), encapsulating human Bone Marrow-Derived Mesenchymal Stromal cells (hBM-MSCs). The gelation time, degradation rate, swelling, morphological and rheological properties of the hydrogels were evaluated, and the effect of COL-II-Tyr content on the viability, adhesion, proliferation, gene expression, and extracellular matrix deposition of hBM-MSCs was assessed.
Results: Increasing the HA-Tyr content led to higher storage modulus and reduced hydrogel shrinkage, resulting in increased swelling. Encapsulated hBM-MSCs survived well in all the hydrogels. Incorporating COL-II-Tyr into HA-Tyr hydrogels created a more favorable microenvironment for hBM-MSCs chondrogenic differentiation. Compared to HA-Tyr alone, the hybrid HA-Tyr/COL-II-Tyr hydrogel promoted enhanced cell adhesion, spreading, proliferation, and upregulation of cartilage-related gene expression.
Conclusion: The injectable HA-Tyr/COL-II-Tyr hybrid hydrogels benefits from the enhanced mechanical strength of HA and cell adhesive, proliferative and chondrogenic conductive properties of COL-II, mimicking the natural cartilage extracellular matrix. These results highlight the promising potential of this hybrid system as a biomaterial scaffold for cartilage regeneration applications, delivering cells in a supportive and bioactive microenvironment.
Keywords: Biomimetic Materials, Cell Encapsulation, Tissue Engineering

Ps-123: Harnessing the Regenerative Potential of Stem Cells: A Systematic Review of Emerging lncRNA-Driven Therapies for Alzheimer's Disease

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Objective: Alzheimer's disease (AD) is a severe neurodegenerative condition marked by progressive cognitive decline and neuronal loss. Despite extensive research, current treatments only provide symptomatic relief, necessitating more effective therapeutic approaches. Recent advancements in stem cell biology and Long Non-Coding RNA (lncRNA) research offer promising avenues for regenerative therapies in AD.
Materials and Methods: This review aims to consolidate literature on lncRNA-driven stem cell therapies for AD. Through

comprehensive searches in PubMed, Embase, and Web of Science, studies published between January 2010 and April 2024 were identified using relevant keywords. Eligible studies underwent rigorous screening, with data extraction performed by two independent reviewers

Results: From 287 initial articles, 42 met inclusion criteria. These studies investigated various stem cell types, such as mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), and neural stem cells (NSCs), for AD treatment. LncRNA-modulated stem cells demonstrated therapeutic potential in AD animal models. For instance, preconditioning MSCs with lncRNAs enhanced their neuroprotective and anti-inflammatory properties, while iPSC-derived neural progenitor cells overexpressing specific lncRNAs promoted neuronal differentiation and survival.

Conclusion: This systematic review underscores the promising prospects of lncRNA-driven stem cell therapies for AD. By leveraging stem cells' regenerative capabilities and lncRNAs' regulatory functions, these innovative strategies hold promise for neuronal repair, neuroinflammation reduction, and potentially halting cognitive decline in AD. However, further research is imperative to address safety, scalability, and clinical translation challenges.

Keywords: Stem Cells, lncRNA, Alzheimer

Ps-124: Using A Novel Acellular Dermal Matrix (Syn Derm) with Boron/MP for Healing Postoperative Wounds from Removing A Tumor on The Skin

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Objective: Improper healing may result in large and unpleasant skin lesions or scars, particularly on the face, leading to psychological problems. Therefore, proper and effective wound healing is crucial. Using autograft skin repair for wounds is complex and can cause additional cost and pain for the patient. In this study, researchers have investigated using a novel allograft acellular dermal matrix (ADM) with boron and mineral pitch as a skin dressing for treating postoperative wounds from removing basal cell carcinoma (BCC) on the nose skin.

Materials and Methods: The methods are outlined step by step along with the report.

Results: Despite the deep wound, using acellular dermal matrix for healing and wound closure was effective.

Conclusion: The rapid closure of the wound in this particular case is promising and sufficient. The use of Syn Derm for fast healing of deep wounds involving difficult tissues, particularly ADM and Syn Derm, shows promising results on wound healing.

Keywords: Aacellular Dermal Matrix, Postoperative, Syn Derm

Ps-125: Investigating The Levels of Interferon Gamma and Tumor Necrosis Factor in The Cerebrospinal Fluid of Brain Tumor Patients Receiving Allogeneic Natural Killer Cells

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Objective: Types of brain tumors include primary tumors as well as metastatic tumors. Today, immunotherapy with Natural killer cells (NK Cells) and injection of these cells into the tumor site or spinal fluid can be a complementary approach to other existing treatments. However, due to the special condition of these tumors and the high cost of immunotherapy methods, early detection of treatment response or resistance is of particular importance. It seems that cerebrospinal fluid and its protein factors can be a good solution for early detection of treatment response or resistance. In this study, we investigated the relationship between tumor necrosis factor alpha (TNF-a) and Interferon Gamma (IFNγ) levels in patients with brain tumors treated with allogeneic natural killer cells.

Materials and Methods: Interferon gamma and Tumor necrosis factor were measured in 18 cerebrospinal fluid samples of brain tumor patients before and after immunotherapy with natural killer cells by ELISA method and the relationship between the levels of these two cytokines and proteins, LDH, glucose, WBC, NK cells, NKT cells, T cells and MRI results of the patients were evaluated before and after treatment by SPSS.

Results: Significant reductions in IFNγ and Tumor necrosis factors were observed in patients with high-grade malignant brain tumors who were immunotherapy with allogeneic NK Cells. The mean level of TNF-a decreased from 41.99 pkg/ml to 26.60 pkg/ml and the mean level of IFNγ decreased from 83.48 to 28.18 pkg/ml. These reductions were significant in the group that responded well to the treatment.

Conclusion: Given the association between cancer and inflammation and considering IFNγ and TNF-a as two pre-inflammatory cytokines, reduction of these two factors during the course of treatment with NK Cells may indicate a reduction in inflammation and tumor recovery. IFNγ and Tumor necrosis factor may be suitable cytokines for studying the response to treatment in patients with brain tumors treated with NK Cells.

Keywords: High-Grade Glioma, Interferon Gamma, Tumor Necrosis Factor Alpha, Allogenic Natural Killer Cells, Cerebrospinal Fluid

Ps-126: The Associations Between Age and Protein Receptors in Breast Cancer

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Objective: Both women and men are affected by breast cancer, which is one of the most common cancers in life. There is a cluster pattern of breast cancer in Iran. Among the provinces of Iran, there is a difference in the prevalence of age. The rates in the central provinces are lower than in the southeastern provinces of Iran. According to various studies, breast cancer occurs most commonly between the ages of 40 and 49 in Iran. Obesity can impact cancer pathways in two ways: one is through the motor pathway, and the other is through an increase in blood glucose levels. We aimed to evaluate the associations between age and receptor-defined breast cancer (luminal A, luminal B, triple negative, and HER2+) in the south of Iran. The majority

of molecular subtypes were Luminal A subtype (36%), followed by Triple Negative (13%), HER2+ (13%), and Luminal B (5%).
Materials and Methods: A total of 109 female patients with primary breast cancer were collected. 45% of cases were aged <45. logistic regression was used to estimate Odds ratios (OR) and 95% confidence intervals (95% CI).
Results: Breast cancer patients aged>or=45 years old, compared with those ages <45 years old, were at an increased risk of luminal A (OR, 1.7; P: 0.1; 95% CI, 0.78-4.1) and triple-negative tumors (OR =3.4; P=0.07; 95% CI, 0.9-13.1). However, Odds ratios did not appear to vary significantly by age. Age in itself is not an independent prognostic factor.
Conclusion: We did not observe a significant difference between age status (more equal to 45 and less than 45) in patients with Her-2 positive (P=0.6) and luminal B breast cancer (P=0.4).
Keywords: Breast Cancer, Protein Receptors, Age, HER2+

Ps-127: Engineered Scaffolds Combined with Exercise Improve The Treatment of Volumetric Muscle Loss

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Objective: Adult skeletal muscle is a stable tissue that does not undergo cell division. Small injuries can be repaired without causing any inflammatory responses or cell death. Skeletal muscle has a limited ability to regenerate after injury, which may cause volumetric muscle loss (VML). When skeletal muscle is injured, damaged, or exercised, satellite cells are activated from their quiescent state. They then proliferate and fuse into existing fibers to provide new myonuclei or return to quiescence. The intensity of the exercise is a crucial factor in the activation of satellite cells and muscle regeneration. The combination of human amniotic membrane (HAM) and silver nano particle (AgNps) with polycaprolactone (PCL) increases the properties of PCL fibers, which leads to the creation of scaffolds with potential application in skeletal muscle tissue engineering. functional recovery was assessed using the sciatic functional index and gait analysis test.
Materials and Methods: In the past, we fabricated PCL, PCL/AgNps, PCL/HAM, and PCL/HAM/AgNps scaffolds for skeletal muscle tissue engineerin. In this study, we utilized scaffolds combined with exercise to investigate their effect on the skeletal muscle model in rats. functional recovery was assessed using the sciatic functional index and gait analysis test. Hematoxylin and eosin staining was performed for histological tissue examination.
Results: According to *in vivo* results, Groups of PCL/HAM/AgNps and PCL/HAM combined with exercise showed significant improvement in motor abilities compared to groups without exercise.
Conclusion: Using PCL/HAM/AgNps, PCL/HAM combined with exercise can improve skeletal muscle performance.
Keywords: Volumetric Muscle Loss, Polycaprolactone, Human Amniotic Membrane, Exercise

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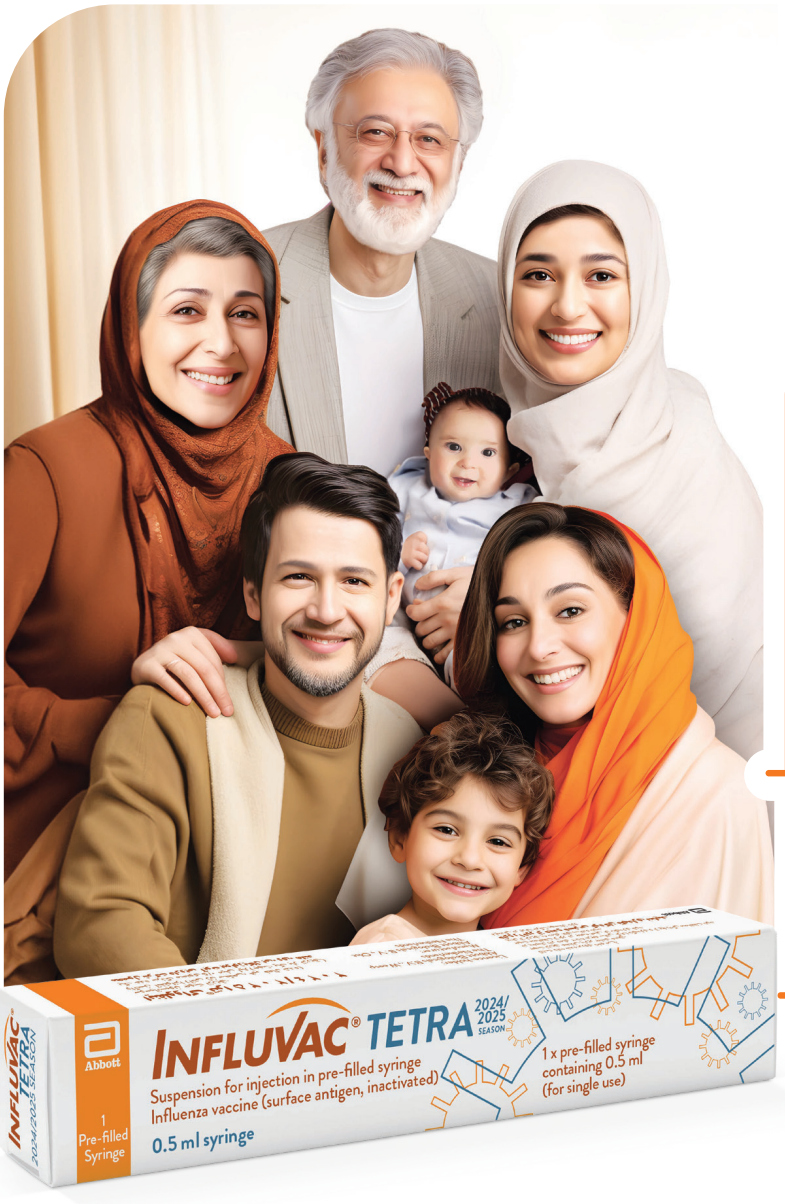

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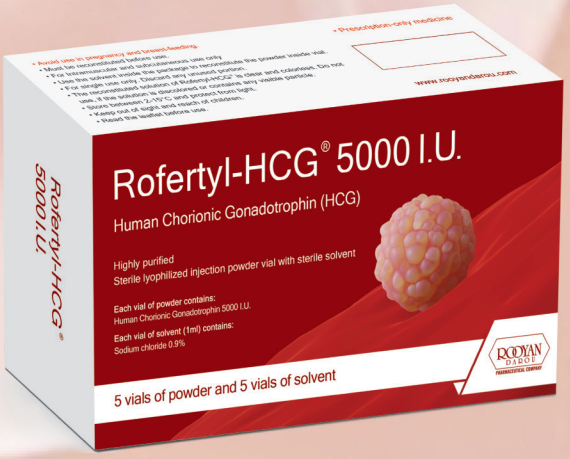

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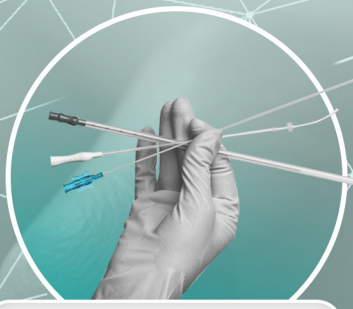

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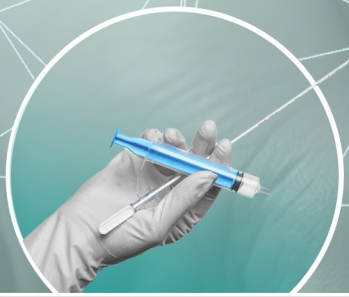

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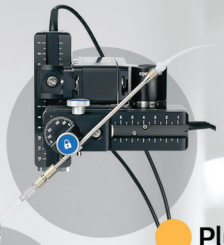

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