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Quality Control and Dosing Regimen Strategy of Wharton's Jelly Mesenchymal Stem Cells (WJMSCs) derived Small Extracellular Vesicles (sEVs)

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Background: Quality control (QC) is an important element in ensuring the safety, efficacy, and quality of the drug substances. The dosing regimen for sEVs can be in the form of protein concentration or the number of particles based on the results of a series of quality controls applied as in-process control. **Methods:** Wharton's Jelly Mesenchymal Stem Cells (WJMSCs) were isolated from the four independent umbilical cord (UC) samples at passage 3 and were characterized as per the International Society for Cellular Therapy guidelines. Small extracellular vesicles (sEVs) were isolated from these four WJMSCs samples at passage 3 using the Tangential Flow Filtration (TFF) and were characterized according to Minimal Information for Studies of Extracellular Vesicles 2018. Based on the QC results for the individually isolated sEVs, the dosing strategy for the in vivo safety study was determined. Each isolated sEvs was standardized and their purity was determined using the ratio of the number of particles to the protein concentration. **Results:** All four independent WJMSCs samples passed the QC tests for the characterization of MSCs. Qualitatively, the presence of sEVs-positive markers using Western blot analysis and bilipid membrane vesicles of sEVs (less than 200 nm) using Transmission Electron Microscopy was detected in all sEVs samples. Quantitatively, the protein and particle concentrations were analyzed and all the sEVs were found to be impure based on the ratio of the number of particles to the protein concentration (< 1.5 x 109 particles/µg protein). All the sEVs preparation showed it contains albumin that may arise from the standard culture medium used during production. **Conclusion:** All sEVs preparations have met the minimum requirement as QC and the dosing regimen for the in-vivo safety study using isolated sEVs was determined using the number of particles instead of protein concentration since the sEVs preparation contains albumin as a contaminant. These sEVs preparations were pooled to be used in a safety study.

Keywords: Quality control; small extracellular vesicles; tangential flow filtration; umbilical cord; Wharton's jelly mesenchymal stem cells

Mesenchymal Stem Cell-derived Extracellular Vesicles for Metabolic Syndrome Therapy: Assessing Efficacy with Nuclear Magnetic Resonance Spectroscopy

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Background: Mesenchymal stem cell derived extracellular vesicles (MSC-EVs), which are membranous vesicles that contain a diverse array of bioactive molecules, encompassing proteins, lipids and nucleic acids have gained substantial attention in the field of regenerative medicine due to its significant therapeutic potential. While a comprehensive remedy for completely eradicating symptoms of Metabolic Syndrome (MetS) symptoms remains elusive, the efficacy of MSC-EVs in improving metabolic parameters in individuals with MetS has prompted researchers to explore this promising avenue further. **Objective:** To raise public awareness regarding the impact of MSC-EVs on the normalization of metabolic parameters in subjects with MetS by conducting literature research. Methods: This study entails a comprehensive review of existing literature concerning the impact of MSC-EVs on metabolic parameters. Additionally, the research will delve into the utility of nuclear magnetic resonance (NMR) spectroscopy for investigating the intricate pharmacometabolomic aspects related to MSC-EV therapy. **Results:** Examining metabolic changes in MetS through NMR spectroscopy is advantageous due to its cost-effectiveness and its ability to allow for the long-term observation of the effects of MSC-EV therapy before transitioning to clinical application. Previous studies demonstrated the potential impact of MSC-sEVs therapy on biochemical reactions within organisms by modulating the metabolite levels. Furthermore, comparing healthy individuals with those with MetS can enhance our understanding of MetS pathophysiology and improve future clinical diagnosis and personalized therapies for MetS. NMR spectroscopy can be employed to explore MetS biomarkers, potential therapeutic targets, as well as to assess how MSC-EVs might enhance the outcomes of specific diseases. **Conclusion:** The effectiveness of MSC-EV therapy in alleviating MetS or the associated diseases has been demonstrated in numerous preclinical studies. Metabolomics analysis using NMR can be a valuable instrument

for understanding these changes and crafting personalized treatments with the use of MSC-EVs for MetS.

Keywords: Mesenchymal stem cells derived extracellular vesicles; metabolic syndrome; nuclear magnetic resonance spectroscopy

The Effect of Nanohydroxyapatite Incorporated with Micro RNA 21 to Regulate Osteogenesis

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Bone is a highly specialized connective tissue with unique property in bone regeneration. Hydroxyapatite due to its bioactivity is widely used in osseous defects to improve osteointegration of bone implants. MicroRNA-21 (miR-21) are endogenously expressed to regulate osteogenesis. Coupling of miR-21 and nanohydroxyapatite (nHA) can be a potential intervention to promote greater and rapid healing of bone fracture. This study investigates the combined effect of miR-21 and nHA scaffold in promoting osteogenesis by regulating the osteoblastic genes Runt-related transcription factor-2, osteocalcin, osteopontin and osteoprotegerin. The growth kinetics and viability of human mesenchymal stromal cells and mineralization activities upon exposure to miR-21 and nHA were studied. Human mesenchymal stromal cells were obtained from Wharton's Jelly of umbilical cord from patients who underwent Cesarean procedure. The human Wharton's Jelly mesenchymal stromal cells (hWJMSCs) were further cultured in osteoinductive media to induce osteogenic differentiation. The hWJMSCc cells were characterized by their tri-lineage differentiation capacity and surface markers expression measured using special staining and flow cytometry respectively. The size and morphology of the nanohydroxyapatite were characterized by dynamic light scattering and field emission scanning electron microscopy. The incorporation of miR-21 onto nHA was verified using confocal imaging and quantified using flow cytometry. A dose curve response was generated for hWJMSCs treated with different concentration of nHA+miR-21 and assessed using Presto Blue assay. Expression of bone markers was evaluated via Western blotting and polymerase chain reaction. The study shows that exogenous miR-21 upregulates bone related gene expressions and osteogenic proteins production confirming its role in osteogenesis. hWJMSCs cells shows no toxicity after treatment with nHA, miR-21 and nHA incorporated with miR-21. Significant increase in alkaline phosphatase was detected in hWJMSCs treated with nHA incorporated withmiR-21 compared with nHA or miR-21 alone. The combination of miR-21 with nHA can potentially have synergistic effect on osteogenesis of hMSCs.

Keywords: Bone formation; miR 21; nanohydroxyapetite; osteogenesis

Bioactivity and Stability Analyses on Polycaprolactone/Hydroxyapatite/Silver Implant Coating

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The increment number of implant failures is attributed to several factors such as infections, age, and limitations of implant materials. Surface modification on implant materials including coating development have been explored to enhance the bioactivity and stability of osseointegrated implant. In this study, a polymer-ceramic composite consisted of polycaprolactone/hydroxyapatite (PCL/HA) and silver (Ag) was successfully coated on titanium alloy (Ti6Al4V) substrates using a dip coating technique. The individual contributions of PCL, HA, and Ag to the coating development were investigated through the bioactivity and stability analyses. The bioactivity of the coating was assessed by immersing the samples in simulated body fluid (SBF) for 7 days, followed by the evaluation of apatite formation on the Ti6Al4V. The scanning electron microscope (SEM) revealed that the HA within the PCL/HA coating promoted apatite nucleation and growth, on the implant coating. The influence of PCL as a binder was demonstrated through the coating's stability analysis, which was tested by immersing the coated Ti6Al4V in distilled water for 1 month. The PCL/HA composite coating substantially improved coating stability. The chemical properties of the coating materials were identified through attenuated total reflectance-Fourier transform infrared (ATR-FTIR), and the coating structure was visualized under SEM. The Ca/P ratio could not be determined since the phosphorus element in the coating rapidly declined following the stability test. The results from the bioactivity and stability analyses showed a promising modification on metallic implant surfaces to address the limitations of implant materials.

Keywords: Bioactivity; hydroxyapatite; implant coating; polycaprolactone; silver; stability

Quantitative Proteomics Analysis of Wharton's Jelly Mesenchymal Stem Cells Secretome Harvested According to Time and Passage

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Wharton's Jelly mesenchymal stem cells (WJMSC) have gained attention as a potential source of therapeutic applications due to their unique properties. These cells, derived from the umbilical cord, possess a high proliferative capacity and the ability to differentiate into various cell lineages. Their secretomes, which consist of a complex mixture of bioactive factors, have shown promising potential in tissue regeneration and immunomodulation. In this study, we aimed to investigate the protein profile of Wharton's Jelly mesenchymal stem cell secretomes harvested at different time points and passages. Wharton's Jelly mesenchymal stem cells were cultured under standard conditions and secretomes were harvested at different time points (24 hours, 48 hours and 72 hours) and passages (passage 3, passage 5, and passage 10). The secretomes were then analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS) to identify and quantify the differentially expressed proteins (DEPs). Our results showed that 62 of proteins were expressed throughout the time and passage points after analysis using Perseus. Each WJMSC secretome profile had distinct characteristics depending on the time and passage points. There were 3 hub proteins were identified in this experiment: collagen

alpha-1, fibulin-1, and transforming growth factor-beta-induced protein across the samples. In conclusion, our study revealed potential proteins involved in Wharton's Jelly mesenchymal stem cell secretomes harvested from different time points and passages. These findings contribute to the understanding of how the properties of Wharton's Jelly mesenchymal stem cells and their secretomes may change over time and different passages, and have important implications for their potential therapeutic applications. Further analysis will be carried out to identify the potential pathways involved which is crucial to understand the effects that secretome may have in a particular treatment.

Keywords: Cell free therapy; mesenchymal stem cells (MSCs); regenerative medicine; secretomes; secretome bioprocessing

Hybrid Gelatin-Pva Bioinks via 3d-Bioprinting for Future Use in Chronic Wound: In Vivo Study

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3D-bioprinting technology is a well-established and promising advanced fabrication technique that utilizes potential biomaterials as bioinks to replace lost skin and promote new tissue regeneration. Currently, cutaneous regeneration biomaterials are preferred over painful skin graft transplants for larger and uneven wound shapes. This study aimed to fabricate biocompatible, biodegradable, and printable bioinks as a cutaneous substitute that leads to newly formed tissue post-transplantation. Briefly, gelatin (GE) and polyvinyl-alcohol (PVA) bioinks were prepared in various concentrations (w/v); GE (6% GE: 0% PVA), and GPVA5 (6% GE: 5% PVA), followed by 0.1% (w/v) genipin (GNP) crosslinking to achieve optimum printability. According to the results, 3D-bioprinted GPVA5_GNP exhibits high swelling ratio capacity with 590.93 ± 164.7% and ideal water vapor transmission rate (WVTR) with <1500 g/m2/h to maintain the moisture of the wound microenvironment. The hydrogels showed excellent interconnected porosity with average pore sizes >100 µm, allowing HDFs to migrate throughout the pores up to 690.0 ± 14.14 µm. Furthermore, 3D-bioprinted GPVA hydrogels were biocompatible to the cells, thereby exhibiting >90% cell viability and attachment activity of human primary dermal fibroblasts (HDFs). It also maintained phenotypic characteristics of HDFs with collagen type-I, vinculin, f-actin, and <30% alpha smooth muscle actin, while expressing >90% Ki67, indicating active proliferative cells. Moreover, the GPVA hydrogels able to support angiogenesis formation and revealed no sign of immune response. Finally, the implantation of 3D-bioprinted hydrogels resulted in improved healing outcomes characterised by superior skin maturity and microstructure features that closely resemble those of native skin. In conclusion, 3D bioprinting does not disrupt the natural characteristics of the hydrogels, which demonstrated the superior properties that are required for the treatment of wound healing.

Keywords: 3D-bioprinting; gelatin; genipin; polyvinyl-alcohol; tissue engineering; wound healing

Comparative Analysis of Marine Collagen Versus Terrestrial Mammals Derived Collagen

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The extracellular matrix (ECM) mostly comprises collagen, which is involved in cell adhesion, growth, and structural support. The study aims to compare the collagen obtained from marine and terrestrial mammalian sources, with attention to factors like stability, source-specific components, extraction techniques, yields, crosslinkers used, and available clinical data. Marine collagen is derived from the swim bladders, skin, muscular tissue, scales, and internal organs of fish, marine animals, and crustaceans. While bovine, ovine, and porcine collagen are the usual sources of terrestrial mammalian collagen. Extraction methods also differ with marine collagen favouring ASC (acid-soluble collagen) and PSC (pepsin-soluble collagen) techniques. Certain crosslinking procedures were used to improve thermal stability, which is important for applications. UV light, bio-crosslinking, carbodiimide, and glutaraldehyde (GTA) are beneficial for marine collagen, which has a denaturation temperature of 37°C. Applying EDC/NHS to lower the rate of enzymatic degradation can also improve collagen obtained from terrestrial mammals. According to extraction efficiency, marine collagen processed with PSC yields 58.3%, whereas collagen processed with ASC yields 35.8%. The yields of collagen extracted from terrestrial mammals are 80.0% (ovine), 75% (porcine), and 74.3% (bovine). Both marine and mammalian collagen have the potential to improve skin health and promote wound healing in clinical settings. To fully understand its unique benefits, direct comparative trials will need to be conducted as marine collagen research is still in its early stages. Marine collagen is emerging as a viable substitute due to hazards associated with terrestrial mammalian collagen such as bovine spongiform encephalopathy (BSE) and religious prohibitions on porcine or bovine collagen among the Jewish, Hindu, and Muslim groups. Considering issues like low heat stability, it's important to remember that developments like crosslinking collagen molecules have opportunities to improve their overall performance.

Keywords: Collagen extraction; cross-linkers; marine collagen; mammalian collagen; wound healing

Fabrication Process Parameters Related to Properties of Thai Silk Fibroin

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Silk fibroin is a natural biodegradable protein which has been generally accepted for its biocompatibility and potential in medical and health applications. The protein has high contents of beta-plated sheet structure, subunits, multiple forms of secondary structures, degradation temperature over 270°C, and the isoelectric point ~ 4. These natural properties can be issues and opportunities for its fabrication processes. Physical and chemical induced gelation and phase separation phenomena of silk fibroin with examples of fabrication process parameters of Thai silk fibroin (Bombyx mori), related to its viscosity, charges, thermal and mechanical stress-responses, stability, degradation and cell responses will be discussed.

Keywords: Biodegradable; natural biomaterial; process parameters; silk fibroin

Physicochemical and Mechanical Characterisation of 3D-Printed Gelatin-Hydroxyapatite for Future Use in Periodontal Regeneration

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Background: Three-dimensional (3D) printing is a promising strategy in addressing current treatments to repair the alveolar bone destruction and restore the functionality of the periodontally involved teeth. This technology provides an advanced approach in fabricating customised complex 3D tissue constructs with specific architectures using the ideal selection of biomaterials. Thus, the right selection and fabrication technique of biomaterial inks are paramount in determining the success of the 3D-printed scaffolds. The study aims to fabricate optimal formulation of gelatin-hydroxyapatite (HA) scaffold for 3D printing and to evaluate the physicochemical and mechanical characterisation assessments of the optimised 3D-printed gelatin-HA. **Methods:** Gelatin-HA scaffolds were fabricated in various concentrations, crosslinked with 0.1% genipin using extrusion-based 3D printing technique. The physical characterisations of such as swelling ratio, biodegradation, contact angles and microstructure of the pore size of the scaffolds were evaluated. Static and dynamic rheological properties of the 3D printed gelatin-HA were also measured. The chemical characterisation including FTIR and EDX as well as mechanical assessment of the scaffolds were also analysed. **Results:** The addition of HA to gelatin increased the swelling ratio, contact angle and pore size of the scaffolds ($p<0.05$) and decreased the biodegradation rate ($p<0.05$). The rheological assessments showed the viscosity of all scaffolds decreased as the shear rate increases. For chemical characterisation, there are no substantial changes in chemical analysis in gelatin-HA. EDX test showed an increase in Ca and P composition with increasing HA concentration in the scaffolds. Mechanical evaluation of the 3D-printed gelatin-HA showed the addition of HA increased the mechanical properties of the scaffolds. **Conclusion:** The addition of HA in 3D-printed gelatin-HA has shown good physicochemical and mechanical properties of the biomaterial ink and has a great potential for periodontal regeneration treatment in future.

Keywords: 3D printing; biomaterial ink; gelatin; hydroxyapatite; tissue engineering

Dual Cell Carrier Systems for Tracheal Tissue Engineering: A Step Towards Facilitating Re-Epithelization and Chondrogenic Differentiation of Human Mesenchymal Stem Cells

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Tissue-based treatments, employing a patient's own cells grown on an extracellular matrix (ECM) derived from donor tissue, offer a promising approach for tracheal structural restoration while minimizing the risk of immune reactions. In this study, the canine trachea was utilized as a tissue model to develop two distinct cell carrier systems for tracheal tissue engineering. First, a decellularized trachea was engineered to support human epithelial cell differentiation. The scaffold demonstrated the presence of essential biochemical niches to support epithelial cell differentiation without cytotoxicity. Simultaneously, we developed an extracellular matrix hydrogel (dECM hydrogel) for the chondrogenic differentiation of human mesenchymal stem cells (hMSCs). This approach involved the injection of a mixture of hMSCs/dECM hydrogel onto cartilage rings locateed on the outer surface of the decellularized trachea. Over a three-week period, the observed chondrocyte-like cells and staining for sulfated glycosaminoglycans (sGAG). indicated successful chondrogenic differentiation. In conclusion, our study demonstrates the remarkable versatility of the decellularized trachea in generating cell carrier systems. These systems hold tial promise for regenerating the epithelial lining and encapsulating chondrogenic lineages, thereby advancing tracheal tissue engineering.

Keywords: Decellularization; extracellular matrix; hydrogel; re-epithelization; tissue engineering; trachea

AML-M5-iPSC-derived Monocytic Cell as A Disease Model: Characterisation of Functional Properties and Drug Responses to Adriamycin

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Acute monocytic leukaemia (AML-M5) is a subtype of acute myeloid leukaemia that often affects children under 2 years old. Astonishingly, the discovery of disease-specific induced pluripotent stem cells (iPSCs) capable of recapitulating human pathogenesis allows us to model this disease with poor prognosis in vitro. In this study, AML-M5-iPSCs were subjected to haemotopoietic differentiation to generate monocytic cells. The monocytic cells were characterised to determine their morphological and functional properties, and compared with their parental cell line THP-1. Their responses towards Adriamycin, a fundamental AML-M5 chemotherapy drug was also investigated. Our results revealed that in terms of size and morphology, both THP-1 and differentiated monocytic cells remained comparable up to 25 days post-differentiation. Within the same duration, their phagocytotic rates also exhibited no significant differences ($p>0.05$) when investigated with carboxylate-modified red fluorescent latex beads. However, cell cytotoxicity assays revealed a significant drug resistance in differentiated monocytic cells towards Adriamycin, the IC50 value was undeterminable even at a high drug concentration of 4 μM after 24 hours of exposure, while the IC50 for THP-1 cell was determined at 0.59 μM ($p<0.01$). Further investigation via cell apoptosis assays also demonstrated that the proportion of healthy cells exhibited a minor decline from 87.1% to 62.5% after 24 hours of drug treatment. This newfound resistance is attributed to the integration of transgenes into the genome of AML-M5-iPSCs, which were reprogrammed using retrovirus. We postulate that the integration of transgenes may interfere with intercalation of Adriamycin into the DNA, thereby inducing less cell death. Despite causing drug resistance to Adriamycin, transgene integration did not seem to alter the morphology and phagocytotic rates of differentiated monocytic cells. In conclusion, AML-M5-iPSCs still hold promise as a valuable disease model but further investigations are warranted to determine the mechanism of transgene-induced drug resistance.

Keywords: Adriamycin; AML-M5-iPSCs; disease model; haemotopoietic differentiation; monocytic cells

Advancements in Hyaluronic Acid-Based Injectable Hydrogel Towards Orthopedic Applications

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Repairing cartilage for degenerative diseases or trauma remains a challenge, as current treatments fall short of promoting cartilage regeneration. To address this, cell-based therapies combined with hydrogels have emerged to facilitate cartilage tissue formation. Here, we introduce a hyaluronic acid-based hydrogel for targeted delivery to knee joint defects. Comprising hyaluronic acid extracellular matrix found in cartilage and stabilizing alginate, this hydrogel undergoes gelation via a Schiff's base reaction between amine groups (-NH2) on hyaluronic acid and aldehyde groups (-CHO) on alginate, forming the HA-Alg hydrogel (HA-Alg hydrogel). Notably, the hydrogel displays shear-thinning properties, supports the chondrogenic differentiation, and holds promise for drug delivery systems that can entrap growth factors during organoid development. Positioned as a non-IVD medical device, the hydrogel has been manufactured in a certified ISO 13485 facilities. To guarantee quality and consistency during pilot-scale production, we implement various quality control measures, including the ninhydrin assay, conductivity measurements, and NMR analysis. Our roadmap for the HA-Alg hydrogel development includes use of

pharmaceutical-grade raw materials, shelf-life testing, and biocompatibility testing. For product design, we have worked with orthopedic surgeons to address the clinical use of the HA-Alg hydrogel in orthopedics and handling the hydrogel in operating room. Collectively, these efforts ensure the successful translation of the HA-Alg hydrogel from laboratory innovation into patients.

Keywords: Cartilage repair; ISO 13485; hydrogels; non-IVD medical device

Enhancing Bone regeneration through the Simvastatin-Loaded Porous PLGA Scaffolds: A Focus on Mechanical Strength Improvement and Drug Release Studies

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Poly(lactic-coglycolic acid) (PLGA) microparticles with simvastatin in a porous structure can result in an abrupt, unregulated increase in drug discharge and a decline in microparticle stability. Improving the therapeutic effectiveness of these carriers requires optimising their structure, drug release rate, and mechanical integrity. **Objective:** This research aims to enhance the architectural, release, and mechanical properties of porous SIM-loaded PLGA microparticles (SIM/PMP) by combining various polymers: chitosan (Chi), pectin (Pec), and pluronic F127 (F127). Methods: A double emulsion solvent evaporation method was used, with two modifications to the conventional approach being investigated. In MM1, biopolymers were added to the internal water phase, while in MM2, they were mixed with the external phase. The samples were freeze-dried and stored for future assessment. **Results**: The results showed that using chitosan at a 1.0% concentration in the SIM/PMP significantly reduced the sudden initial release of SIM, resulting in a consistent release over 21 days. This was confirmed through High-Performance Liquid Chromatography (HPLC). Pluronic F127 significantly enhanced the compressive strength of the scaffolds more than pectin and chitosan. **Conclusion:** Pluronic F127, a synthetic polymer, was found to be the best biopolymer for improving the release profile and mechanical strength of the SIM/PMP scaffolds. This study highlights the effectiveness of specific biopolymers in reducing the typical limitations of porous SIM/PMP microparticles, thereby aiding in the advancement of more sophisticated drug delivery systems.

Keywords: Simvastatin PLGA-loaded microparticles; scaffold; tissue regeneration

Integrase-Free Lentivirus Vectors in The Establishment of Human-Induced Pluripotent Stem Cells

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Background: The potential of reprogramming primary cells to pluripotent stem cells has a great impact on regenerative medicine. Conventionally, viral vectors have been employed for reprogramming cells into induced pluripotent stem cells (iPSCs). However, this can lead to the inclusion of genes into the genome which can have adverse effects in cell functions. This study suggests the generation of iPSCs using non-integrating lentiviral vectors for the transient expression of transcription factors which reduces the risk of irreversibility. Hence, non-integrating viral vectors (NILVs) are expected to have secure profile and highly desirable for clinical use. **Objective:** To establish a human iPSCs from peripheral blood mononuclear cells (PBMCs) using NILV encoding for transcription factors (KLF4, OCT3/4, and SOX2). **Methods:** This study will transduce PBMCs with a cocktail of reprogramming transcription factors using in-house produced NILV. The PBMC-derived iPSC will be further characterized by alkaline phosphatase staining, specific gene markers and embryoid body formation assay. **Expected Outcome:** Reprogramming PBMCs into iPSCs can be done using NILV encoding transcription factors. **Conclusion:** iPSCs derived from this approach can be differentiated into any potential cell type and transplanted for treatment purposes without the risk of genomic alterations.

Keywords: Induced pluripotent stem cells; non-integrating lentiviral vectors; reprogramming; peripheral blood mononuclear cells; transcription factors

Unravelling the Potential of Transdermal and Topical Delivery of Wharton's Jelly-Derived Stem Cell Secretome for Atopic Dermatitis Management

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Atopic dermatitis (AD) is a common chronic inflammatory skin disorder that affects millions of children and adults' worldwide. Similar to most skin inflammatory disorders, the pathogenesis of AD remains unclear, however it has been characterized as an intense itching and repeated eczematous lesion. Recent technology advancements have led to the development of products aimed at addressing different aspects of AD, such as alleviation of symptoms, reduction of inflammation and itching, and the restoration of skin barrier. These products include topically applied treatments, oral drugs, biological therapies, and phototherapy. The secretome derived from Wharton's jelly mesenchymal stem cell (WJ-MSC), comprises of different types of bioactive molecules such as cytokines, growth factors, and extracellular vesicles. These components have potential therapeutic benefits in various medical conditions, including skin wound healing and AD. Furthermore, the secretome of WJ-MSC has been found to exhibit angiogenesis properties and has been successful in promoting skin wound healing, offering similar benefits in the treatment of AD. By using encapsulated secretome derived from WJ-MSC and inserting it into a transdermal patch, it allows the bioactive molecules to have a more targeted delivery to the affected areas, making it a promising approach for regenerative medicine applications. The integration of natural bioactive compounds, such as Naringenin and Quercetin, in the transdermal patch can further enhance its therapeutic potential. Transdermal patches have emerged as a promising delivery system, offering non-invasive and controlled release of drug delivery and bioactive compounds. This research aims to develop a novel transdermal patch containing natural bioactive compounds, encapsulated secretome derived from WJ-MSC, and biomaterials like collagen and hyaluronic acid. This research represents a multidisciplinary approach that integrates advancements in stem cell and biomaterial research with new innovative insights in treating AD.

Keywords: Atopic dermatitis, eczema; secretome; skin inflammation; transdermal patch; Wharton's jelly mesenchymal stem cells

The Fabrication of Gelatin-Elastin-Nanocellulose Composite Bioscaffold as a Potential Acellular Skin Substitute

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A porous biological scaffold that acts as an acellular skin substitute is a viable method for chronic wound management. Gelatin has the potential as a biomaterial for developing biological scaffolds. However, gelatin usage is limited due to its lack of enzymatic and thermal resistance, as well as mechanical weakness. Hence, gelatin requires cross-linking and reinforcement with other materials. This study aimed to fabricate and characterise composite scaffolds composed of gelatin, elastin, and cellulose nanocrystals (CNC) and crosslinked with genipin. The scaffolds were fabricated using the freeze-drying method. The composite scaffolds were composed of different concentrations of CNC, whereas scaffolds made of pure gelatin and a gelatin–elastin mixture served as controls. The physicochemical and mechanical properties of the scaffolds, and their cellular biocompatibility with human dermal fibroblasts (HDF), were evaluated. The composite scaffolds demonstrated higher porosity and swelling capacity and improved enzymatic resistance compared to the controls. Although the group with 0.5% (w/v) CNC recorded the highest pore size homogeneity, the diameters of most of the pores in the composite scaffolds ranged from 100 to 200 µm, which is sufficient for cell migration. Tensile strength analysis revealed that increasing the CNC concentration reduced the scaffolds' stiffness. Chemical analyses revealed that despite chemical and structural alterations, both elastin and CNC were integrated into the gelatin scaffold. HDF cultured on the scaffolds expressed collagen type I and α-SMA proteins, indicating the scaffolds' biocompatibility with HDF. Overall, the addition of elastin and CNC improved the properties of gelatin-based scaffolds. The composite scaffolds are promising candidates for an acellular skin substitute.

Keywords: Composite bioscaffold; elastin; gelatin; nanocellulose; skin substitute

Numerical Study of Propagation and Standing Surface Acoustic Wave (SAW) on Cellular Stress

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Surface Acoustic Waves (SAWs) are versatile sound waves traveling along elastic surfaces, with significant applications in biology, medicine, and materials science. Their potential for cellular manipulation underscores the necessity for understanding their interactions with cells. However, the precise mechanisms of SAW-induced cellular stress and biological responses remain unclear, necessitating a robust analytical approach. This study aims to develop and validate a numerical model to analyze SAW device characteristics and their cellular interactions, quantifying induced cellular stress and elucidating biomechanical processes. A multiphysics computational model integrates cellular biomechanics with wave propagation dynamics, simulating SAW generation using two ports of interdigital transducers (IDT) on piezoelectric substrate which separated by a delay line. Finite Element Method (FEM) solutions analyze stress distribution within cellular constructs, with parametric studies exploring frequency, delay line, input voltage and cellular properties' effects on stress patterns. Results reveal diverse stress distributions, influenced by wave characteristics and cell mechanics. Lower frequencies, shorter delay line and higher input voltages produce widespread stress. This complex interplay significantly impacts cellular responses, including deformation and internal stress. The study offers a comprehensive computational framework for understanding SAW-cell interactions, aiding in SAW-based device optimization for biomedical engineering applications. Insights into stress distribution and cellular responses advance cell mechanics understanding, benefiting tissue engineering, drug delivery, and cellular manipulation.

Keywords: Cellular stress; finite element method; surface acoustic waves

Oral Tissue-derived Stem Cell Response to Material Topography

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Stem cells' role in tissue regeneration is undoubtedly important. Two approaches are known. Inducing host-stem cells to differentiate into the subjected lineage or delivering donor-stem cells and inducing them afterward. Oral tissue has the potential as a stem cell source, and these cells are proven to have pluripotent characteristics, thus being able to be used to regenerate different kinds of tissue or even organs. For this purpose, directing stem cells into a specific lineage is needed. Different strategies can be performed, but all have the same goal, to provide a correct cue. In this paper, we discussed topographical cues from material that hypothetically directs stem cell differentiation.

Keywords: Cell-material interaction; differentiation; morphology; pulp-derived stem cell

Kapok Fiber: A New Natural Biomaterial for Versatile Applications

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Kapok is a short cellulosic fiber retrieved from the seedpod of kapok (Ceiba pentandra) tree. Kapok tree of the Bombacaceae family is widely cultivated in Southeast Asia, and some parts of East Asia and Africa. In Thailand, kapok tree can be widely grown in all regions. This natural fiber is apparently considered as the lightest fiber in the world (six times lighter than cotton) due to its hollow structure with large lumen and thin cell well. The outer surface of fiber is covered with a layer of wax, presenting its hydrophobic/oleophilic characteristics and great water repellency. In addition, its large lumen significantly contributes to its sorption capacity. Due to such unique characteristics of kapok fiber, it was reported in various applications. In the ancient time, it is conventionally used as stuffing materials for beds and pillows. Water-safety equipment (life preservers) can also made of kapok fiber because of its buoyancy properties. Its potential as absorbent material was well reported for oil, dye, metal ion, and sound, for example. It was also applied as template material in photocatalysis and catalysis, reinforcement material, and encapsulating material for thermal energy storage. In our work, we are first to report the biocompatibility of kapok fiber and its potential use as scaffolding to support cell growth. This reveals kapok fiber as a potential biomaterial for future investigation in biomedical and healthcare applications.

Keywords: Biocompatibility; characteristics of kapok fiber; kapok fiber

The Role of Aligned Nanofibers of Nerve Conduit Seeded With Schwann-Cell Like Cells in Modulating Neuropathic Pain and Inflammation

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Neuropathic pain, resulting from peripheral nerve injury, causes spontaneous burning or stabbing sensations, significantly impacting quality of life. Current treatments like antidepressants and opioids manage symptoms, not causes. While autologous nerve grafting is effective for nerve reconstruction, it leads to donor-site morbidity. Artificial nerve conduits show promise in bridging nerve gaps and aiding regeneration, especially when combined with mesenchymal stem cells (MSC). MSCs, with their ability to release growth factors and modulate immune responses, offer analgesic effects in animal studies. Seeding MSCs onto nerve conduits enhances cell proliferation, promoting nerve recovery and reducing neuropathic pain. This study aims to determine the role of aligned nanofibers of nerve conduit on the secretion of inflammatory cytokines and pain mediators by neural-differentiated MSC. We hypothesize that nanofiber orientation will impact cell morphology and behavior, thereby affecting its ability to mediate inflammation and neuropathic pain. Objective: To elucidate the role of seeding Schwann cell-like cells (SCLC) and nerve conduit nano-topography in modulating inflammation and neuropathic pain. Methods: Firstly, MSCs will be induced to differentiate into SCLCs. Subsequently, these SCLCs will be seeded onto nerve conduits with either random or aligned nanofibers. Finally, an indirect co-culture of SCLC-seeded nerve conduits with activated macrophages will be conducted. Expected Outcome: SCLCs seeded on different nanofiber orientations will exhibit distinct cell morphology and secretion profiles of inflammatory cytokines and pain mediators, as well as varying potential to polarize naive macrophages (M0) into anti-inflammatory macrophages (M2). Conclusion: This study will be able to elucidate the role of nanofiber orientation in modulating the potential of SCLCs to mediate inflammation and neuropathic pain.

Keywords: Mesenchymal stem cells; nerve conduit; neuropathic pain

Effects of Mesenchymal Stem Cell-Derived Extracellular Vesicles on Skin Fibroblasts and Melanocytes

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Research has unveiled the advantageous qualities of extracellular vesicles present in conditioned media from umbilical cord-derived mesenchymal stromal cells (UC-MSCs), encompassing attributes such as wound healing, re-epithelialization, and skin rejuvenation. Nevertheless, further investigations are imperative to delve into the specific effects of small extracellular vesicles derived from UC-MSCs (UC-MSC-sEVs) on the skin, particularly concerning their anti-scarring properties, skin rejuvenation capabilities, and skin-whitening effects. This study aims to scrutinize the efficacy of UC-MSC-sEVs in regulating the synthesis of the skin's extracellular matrix (ECM) and pigmentation in vitro. UC-MSC-sEVs were isolated, characterized, and their impact on the proliferation, migration, antioxidant activity, and ECM gene expression of human dermal fibroblasts (HDFs) were assessed. Additionally, we explored the influence of UC-MSC-sEVs on the proliferation, melanin content, and tyrosinase (TYR) activity of human melanoma cells (MNT-1) to evaluate their potential in inhibiting hyperpigmentation. Results indicated a positive effect of UC-MSC-sEVs on HDF proliferation, with no discernible changes in cell migration, superoxide dismutase activity, or collagen 1 and 3 expression levels. However, an increase in the gene expressions of fibronectin, matrix metallopeptidase (MMP) 1, and MMP3 was observed. While sEVs did not impact MNT-1 cell proliferation, they effectively suppressed melanin synthesis without affecting TYR activity. Moreover, topically applied sEVs were localized within the stratum corneum layer. These findings underscore the potential of UC-MSC-sEVs in enhancing HDF proliferation, modulating ECM gene expression, and reducing melanin synthesis.

Keywords: Extracellular vesicle; fibroblast; melanocyte; mesenchymal stem cells; skin

Biofilm for Wound Healing Application

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Typically, wet-to-dry dressing is utilized to treat wounds, and the function of wound materials is to create and maintain a moist environment with optimal conditions. Alginate is one of the biopolymers opted as the wound materials. It is a non-woven, non-glue cushion and strips made of polysaccharide extracted from brown seaweed. Interestingly, this biopolymer achieves its clinical via a unique mode of action, allowing it to absorb a large amount of exudate up to 20 times its weight. However, alginate does not have antibacterial properties that protect agents with particular value in treating skin wounds. Therefore, materials ranging from oxide to plant-derived were incorporated with alginate. The assessment of the antibacterial properties of the biofilm was carried out via the disc diffusion method. Zinc oxide was embedded in the alginate matrix using a solution-casting technique. This biofilm gave promising results when it was resistant and susceptible to Staphylococcus aureus and Escherichia coli. It was proven that zinc oxide caused damage to bacterial cell walls by inducing reactive oxidative stress. Also, there were attempts to fabricate a biofilm of alginate with curcumin. Curcumin is a bioactive compound derived from Cucurma longa or also known as turmeric. It was also found to have the ability to disrupt the bacterial cell wall integrity. Unfortunately, the low concentration of curcumin applied in the fabrication of alginate biofilm led to no resistance to the Staphylococcus aureus. It seems that the concentration of antibacterial agents plays a vital role as well. Remarkably, it shows that there is a wide potential for materials that act as antibacterial agents to be considered in wound healing applications.

Keyword: Alginate; antibacterial properties; curcumin; zinc oxide

A Novel Study of Phytochemical Analysis and Functional Effects of Seabuckthor*n (Hippophae Rhamnoides. L)* on Immune Cell Cultures

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This research is aimed to identify ingredients and quantitation of bioactive components that will eventually allow the screening evaluation of functional impacts of seabuckthorn (Hippophae rhamnoides.L). Objective of the study was to develop a simple, precise and accurate high performance liquid chromatography (HPLC) method, for the determination of vitamin families in seabuckthorn by HPLC, DAD with C18 (100 x 4.6 mm; 5 µm) column were used. The proposed method was successfully applied to analysis mixture of five water-soluble vitamins in seabuckthorn. Recently we identified an analysis which PCR based method RAPD (Rapid Amplified Polymorphic DNA) to study genetic diversity in the seabuckthorn. Our model which stimulated peripheral blood mononuclear cells (PBMC) with lipopolysaccharide (LPS) helps us for further study of immune effective foods to spread a broad spectrum on innate immunity and T cell related mechanisms such as activation of CD4, CD8 and biological important cytokines, mediators. Taken together, seabuckthorn is the best nutritional/ medicinal source for the human and the commercialization of these individual products would be a great achievement in alternative nutritional diet sources.

Keywords: Genetic variation, immune enhancement; liquid chromatography separation; seabuckthorn; vitamins

Extraction of Hydroxyapatite and Gelatin from Black Tilapia Fish

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Hydroxyapatite (HAp) is a calcium phosphate biomaterial chemically similar to the mineral component of bones in the human body. It is used as a filler to replace damaged bone or as a coating on implants in orthopaedic and dental applications. HAp is normally produced through the chemical synthesis method. This method might be complicated, expensive and time-consuming. HAp has been extracted from black tilapia bones and scales (a waste product from a fishery factory) using a simple heat treatment method (800 to 1200˚C). Hydroxyapatite obtained from animal bone has the advantage due to the preservation of raw material properties such as chemical composition (calcium phosphate). Black tilapia (freshwater fish) was identified to have a high potential to produce hydroxyapatite from its bones and scales. HAp from black tilapia is an option for patients to use a halal product for biomedical applications. Gelatin, or collagen derivative, is a brittle, colourless and translucent solid substance. It is a biopolymer used extensively in various industries such as food, pharmaceutical, and photographic. In the food industry, gelatin acts as an ingredient to provide chewiness, texture, stabilisation, gelling and emulsifying properties in confectioneries and dairy products. Gelatin is also accepted and applied widely in the medical field as it dissolves and is absorbed easily within the human body. Gelatin sourced from pig skin and bovine hides is used abundantly worldwide and is also said to be the most commercial type of gelatin. Gelatin extracted from the fish (bones, scales and skins) is an alternative resource besides mammalian animals. The extraction process from black tilapia bones, scales and skins was carried out through the use of hydrochloric acid (HCl) with different concentrations followed by a final extraction with water at 50˚C for several hours and ended with drying. The black tilapia fish (bones, scales and skin) is found to be a source of halal gelatin with good chemical and functional properties.

Keywords: Black tilapia; bone; gelatin, hydroxyapatite; scale and ski

Effect of Cross-linking Strategies on Mechanical Traits for the Formulation of New Bioinks to Mimic Human Skin

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Treating full-thickness skin injuries remains a challenge in medicine. While three-dimensional (3D) bioprinting shows promise for crafting skin replacements, finding bioinks with the needed strength, printability, and compatibility is critical. This study aims to bridge this gap by focusing on replicating the mechanical characteristics of human skin layers using diverse crosslinking methods in bioink formulations. By targeting the elastic moduli of skin layers, the goal is to advance bioengineered skin tissues that closely mimic natural skin traits. The bioink samples were carefully formulated to systematically investigate the effects of varying concentrations of key components: Gelatin(Gel), alginate(Alg), and polyethylene glycol diacrylate(PEGDA), on their mechanical properties. Precise adjustments in Gel(0.5%-1%), Alg(1%-4%), and PEGDA(2%-10%) concentrations allowed for the creation of distinct samples. Initiating photo-crosslinking with photoinitiators, followed by UV exposure, was complemented by the incorporation of glucono-δ-lactone (GDL) and calcium carbonate ($CaCO_3$) to facilitate the gelation process. Ensuring crosslinking and structural stability, an overnight incubation period significantly influenced the final mechanical properties. Lower concentrations yielded softer mechanical profiles resembling the hypodermis(~16-50 kPa), while higher concentrations approached dermis levels(~150-300 kPa). The Gel1-Alg4-PEGDA10 formulation demonstrated the highest mechanical strength among the tested bioink samples. Various crosslinking approaches were applied to this formulation to replicate the Young's modulus of the epidermis. UV exposure after 24 hours of room incubation resulted in the highest Young's modulus akin to epidermis(>1 MPa). Room incubation alone showed a moderate modulus. Moreover, altering the timing of UV exposure following different incubation periods significantly impacted Young's modulus. In this study, the intricate modulation of bioink properties through meticulous formulation and strategic crosslinking revealed a spectrum mirroring diverse skin layers. Gel1-Alg4-PEGDA10 displayed remarkable strength, emphasizing the impact of varied concentrations and crosslinking strategies. This nuanced understanding offers promising avenues for faithfully replicating natural skin, pivotal in addressing severe skin injuries.

Keywords: Bioink; crosslinking-strategies; human skin layers; tissue engineering

MECHASCAN - Novel Real-time Non-invasive Optical Imaging Modality for Mechanical Assessment of Organoids, Engineered Tissue and In Vivo Animal Models

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Introduction: Tissue engineering holds great promise for understanding tissue function, disease modeling, and tissue replacement. Monitoring the mechanical properties of engineered grafts during culture is crucial for their development and function. This abstract introduces a novel modality called Optical Coherence Tomography for Engineered Tissue (OCTET) with the MechAscan post-processing algorithm, enabling non-invasive and sterile assessment of tissue mechanical properties in multi-well culture conditions and high throughput screening. **Methods:** Agarose hydrogels with varying concentrations were imaged using OCTET, and the mechanical properties were analyzed using MechAscan. Young's Modulus was calculated through compression mechanical testing. Validation of the agarose gels was carried out using compression testing and the OPTICS11 Life Pavone nanoindentation instrumentation. The range of material stiffness and the ability to assess materials with varying stiffness such as gradients was also assessed using MECHASCAN. Human liver-derived organoid, AAV8.TBG.Cre-treated hepatic senescence and CCl4-induced liver fibrosis studies were investigated using Mechascan. Organoids were monitored on days 4, 7 and 14 (n=5/group) during maturation. In animal experiments, mice were euthanised according to UK Home Office regulations, respectively, on day-7 (n=2/group) and weeks 4 and 12 (n=3). **Results & Discussion:** The study revealed the mechanical properties of agarose gels through nanoindentation testing and OCTET analysis, establishing a calibration curve for subsequent assessments. Investigation of stiffness changes in both animal and engineered tissue and hydrogels using Mechascan with OCTET monitoring revealed changes in mechanical property aiding in the monitoring of tissue development and behavior. The evaluation of GelMA hydrogels showed a decrease over time. In the AAV8.TBG.Cre-induced hepatic senescence injury model shows different levels of injury related to the applied dose. In CCl4-induced liver fibrosis, mice at 4-weeks exhibit early-stage fibrosis, and those at 12 weeks show significantly advanced chronic fibrosis. Fatty and healthy liver organoids results indicate the difference in relative stiffness between the two groups to the

imaging time point. **Conclusion**: The results obtained from the intensity information of the imaging data and the wavelength values deduced from this information demonstrated the ability of Mechascan for non-destructive spatial mechanical assessment of engineered constructs and animal tissues across tissue with variable stiffness such as liver tissues with fibrosis and tumour formation.

Keywords: Liver organoids; liver tissue; online monitoring; optical coherence elastography, stiffness