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BOOK OF ABSTRACTS

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Engineering a Vascularized Hypodermal Tissue: Optimization of 3D Organ-on-Chip Parameters for Biomimetic Skin Models

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Introduction

Human-relevant skin equivalents are increasingly needed in regenerative medicine as experimentally tractable platforms for therapeutic testing, helping to reduce reliance on conventional animal models. However, current skin models frequently omit the hypodermis layer or lack functional verification. Consequently, biofabrication of a vascularized hypodermis remains a major hurdle in developing full-thickness skin equivalents. The study aimed at modeling functional, vascularized hypodermal tissue model using a microfluidic system.

Materials & Methods

The interaction between human adipose-derived stem cells (ASCs) and human umbilical code vein endothelial cells (HUVECs) was evaluated. First, we systematically tested medium compositions and cell seeding ratios. The optimized parameters were then applied across two-dimensional direct co-culture, two-dimensional indirect transwell systems, and three-dimensional organ-on-chip platforms. (Lastly, we designed a prototype of full-thickness skin model incorporating engineered hypodermis using collagen-fibrinogen matrices).

Results

Two-dimensional direct co-culture resulted in extensive cell death, demonstrating three-dimensional architecture is essential for ASC-HUVEC coexistence. In three-dimensional organ-on-chip culture, AGM:EGM-2 ratio of 1:3 optimally balanced angiogenesis and adipogenesis. Reducing ASC:HUVEC ratio to 1:11 prevented ASC dominance and yielded robust vascular networks with clear lumens. Immunofluorescence confirmed perivascular adipogenesis, with BODIPY-positive lipid droplets accumulating within α-SMA -positive perivascular ASCs. Transwell experiments showed no notable paracrine effects, indicating that 3D architecture and direct cell interactions are essential for functional perivascular adipogenesis.

Conclusion

Engineering vascularized hypodermal tissue requires three-dimensional architecture and precisely balanced cell-medium conditions. This optimized protocol provides a physiologically relevant platform for investigating the cellular interactions required to engineer functional, vascularized hypodermal tissue.

Neurally primed mesenchymal stromal/stem cell-derived small extracellular vesicles as a regenerative candidate for multiple sclerosis

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Introduction

Multiple sclerosis (MS) is a chronic neuroinflammatory and neurodegenerative disease with limited treatment options for progressive disability. Mesenchymal stromal/stem cell-derived small extracellular vesicles (MSC-sEVs) are emerging as a promising cell-free therapeutic strategy, but it remains unclear how lineage priming of MSCs influences sEV cargo and regenerative activity in a CNS-relevant context. We hypothesised that priming MSCs toward neural-like and glial-like states would generate sEVs with distinct molecular signatures and enhanced pro-repair properties.

Method

Human bone marrow-derived MSCs from progressive MS donors were expanded and primed for 3 weeks toward neural-like (nMSC) or glial-like (gMSC) phenotypes. sEVs were isolated by differential ultracentrifugation and characterised by transmission electron microscopy, nanoparticle tracking analysis, and proteomic marker profiling in accordance with MISEV recommendations. Cargo composition was analysed by DIA LC-MS/MS proteomics and miRNA sequencing. Functional activity was assessed in a primary rat cortical scratch assay using live-cell imaging.

Results

Primed cultures exhibited reduced proliferation, morphological alterations, and distinct whole-cell proteomic profiles. Isolated vesicles displayed expected sEV morphology and size distribution, enrichment of canonical exosomal markers, and depletion of major intracellular contaminants. Proteomic and miRNA analyses demonstrated broad priming-associated cargo remodelling, including enrichment of RNA- and translation-related pathways and distinct signatures in neural- and glial-primed sEVs. In the scratch assay, both nMSC-sEVs and gMSC-sEVs significantly increased the wound closure rate relative to baseline, whereas unprimed MSC-sEVs did not.

Conclusion

These findings show that lineage priming reshapes MSC-sEV cargo and is associated with enhanced in vitro repair activity, supporting further investigation of lineage-primed MSC-sEVs as regenerative therapeutics for MS.

Rethinking Limbal Stem Cell Deficiency

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Introduction

Limbal stem cell deficiency (LSCD) is a severe ocular surface condition characterized by impaired regeneration of the corneal epithelium due to loss or dysfunction of limbal epithelium stem cells. This results in corneal opacity and progressive vision impairment. Current treatment options remain insufficient, underscoring the need for better understanding of the disease mechanisms across different LSCD etiologies.

Purpose

To compare and characterize three different LSCD models, in order to identify shared and distinct pathogenic features.

Method

LSCD was induced in the animal model using three approaches: mechanical corneal epithelial removal, alkali burn, and suture placement. Immunofluorescence staining of tissue sections was performed using antibodies against keratin 12, keratin 13 and ΔNp63, to assess epithelial phenotype and limbal stem cell presence. Gene expression was analysed by quantitative PCR, targeting 20 selected genes with roles in inflammation, angiogenesis and wound healing.

Results

In non-treated rats, K12 was detected in the cornea, K13 in the conjunctiva and ΔNp63 in the basal layer of the limbal epithlieum and the cornea. Animal subjected to the different injury showed less expression of K12, more of K13 and reduced ΔNp63. Quantitative PCR analysis showed significant upregulation of several target genes in the alkali group, with notable differences also in the suture and mechanical groups, indicating distinct molecular responses across the different LSCD models.

Conclusion

The selected immunohistochemical markers, K12, K13 and ΔNp63 effectively characterize corneal epithelial changes associated with LSCD, while qPCR analysis further supports distinct molecular responses across experimental models.

Exogenous Modulation of Wnt and Notch Signalling for Dental Tissue Regeneration

Ola Mustafa

Introduction

The Wnt and Notch signalling pathways are key regulators of cell fate, proliferation, and tissue homeostasis. Their activity plays an essential role in tooth development and dentin–pulp regeneration by influencing dental pulp stem cell (DPSC) behaviour. While experimental modulation of these pathways has provided important insights into stem cell biology, many studies rely on compounds with limited clinical applicability, creating a translational gap between laboratory findings and potential therapeutic use. Identifying molecules that can safely and effectively influence these pathways in human DPSCs is therefore an important step toward advancing regenerative dentistry.

Materials and Methods

This study investigates clinically relevant small molecule modulators of Wnt and Notch signalling and their effects on human DPSCs in vitro. DPSCs are characterised to confirm their mesenchymal stromal cell phenotype using flow cytometric analysis of surface marker expression and assessment of trilineage differentiation potential. Following characterisation, cells are exposed to selected pathway modulators. Cellular responses are evaluated using molecular approaches, including gene expression profiling related to pathway activity and odontogenic differentiation.

Results and Conclusion

Flow cytometric analysis supports the expected mesenchymal stromal cell phenotype of the DPSCs. Ongoing analyses examine how modulation of Wnt and Notch signalling influences odontogenic differentiation and mineralised matrix formation. This work aims to establish a clinically relevant framework for guiding dental stem cell fate and to support the development of regenerative strategies for dentin–pulp tissue repair.

NAA60 loss of function variants causing neurological phenotypes and primary brain calcification from young age

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Introduction

Recently, NAA60 was identified as a gene associated with primary brain calcification (PBC), thereby making it the seventh gene associated with this heterogeneous disorder. PBC is characterized by calcium deposition in the brain and may cause progressive neuromuscular, psychiatric, and cognitive symptoms. So far, only a few individuals with NAA60 variants have been described. Therefore, additional case reports and functional studies are needed to further describe the pathophysiological role of NAA60 in PBC.

Methods

We reviewed all published NAA60 variants and families and identified three additional cases with pathogenic NAA60 variants. Notably, all individuals presented here are relatively young, and global developmental delay and cognitive impairment appear to precede the classical symptoms of brain calcification.

Results

In this study, we describe additional individuals with previously unreported NAA60 variants and perform functional experiments to assess their impact. Our assays show that the variants impair NAA60 function through several mechanisms, including reduced enzyme activity, decreased protein stability, and altered cellular localization. Future studies using advanced cell models may clarify how NAA60 dysfunction contributes to neurological disease.

Conclusion

Taken together, our findings indicate that loss of N-terminal acetylation of membrane proteins is likely a central factor in the PBC pathogenesis. These results link NAA60 to neurological disease, support its inclusion in the genetic work-up of PBC, and underscore its potential role in neurological development, which may enable earlier diagnosis and prevention of PBC.

Organ-on-Chip Fabrication for Dentoalveolar Tissue Modeling

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Introduction

In the field of tissue engineering, organ-on-chip (OoC) technology has become a powerful tool for dental modeling, allowing physiological processes to be observed with greater control and precision compared to traditional cultures. This study aimed to develop a two-chamber PDMS-based microfluidic chip using soft lithography and evaluate co-culture-driven cell interactions representing different dentoalveolar tissues.

Materials & Methods

Master molds were fabricated on silicon wafers via soft lithography to produce two-chamber PDMS chips. Custom polycarbonate lids were designed and assembled to seal the devices. Two co-culture systems—human umbilical vein endothelial cells (HUVEC) with dental pulp stem cells (DPSC), and HUVEC with periodontal ligament stem cells (PDLSC)—were introduced into separate chambers. Cultures were maintained for 5 days under standard conditions. Following incubation, immunofluorescence staining was performed using CD31 to assess endothelial structures, phalloidin for cytoskeletal organization, and DAPI for nuclear visualization.

Results

Both co-culture systems demonstrated robust cell viability and organization within the microfluidic environment. Distinct microvascular-like networks were observed, particularly in HUVEC-containing cultures, as confirmed by CD31 expression. Cytoskeletal staining revealed well-defined cellular morphology, and DAPI confirmed uniform cell distribution. Notably, evidence of interaction between chambers was observed, suggesting effective communication or signaling across the chip design.

Conclusion

The developed PDMS-based two-chamber organ-on-chip system successfully supported co-culture growth and microvascularization. The platform demonstrates potential for studying intercellular interactions and vascular development in engineered microenvironments, with applications in tissue engineering and disease modeling.

Exploring Human Dental Pulp Stem Cells for Neural Tissue Regeneration

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Introduction

Neural crest-derived Dental Pulp Stem Cells (DPSCs) are a promising candidate for neural tissue regeneration. However, most of the conventional studies utilized standard 2D monolayer cultures, which failed to model the complex 3D microenvironment mimicking in vivo cell architectures and functionalities.

Aim

This study aimed to validate the hypothesis that human DPSCs exhibit plasticity supporting both neurogenic differentiation into self-assembling 3D neurospheres and a supportive angiogenic potential for neural tissue regeneration.

Methodology

Biobanked human DPSCs were characterized as mesenchymal stem cells (MSCs) via immunophenotyping and multilineage differentiation. Following induction in neurogenic (NGM) or endothelial (EGM) growth media, lineage-specific marker expression was analyzed using flow cytometry and confocal microscopy. Targeted RNA analysis was performed to evaluate the nNOS-signaling pathway in NGM-induced cells. 3D neurogenic potential was further investigated by monitoring neurosphere size with a live-cell imaging system as well as neurosphere formation on micropatterned surfaces. Endothelial/angiogenic functional capacity was assessed via a 3D Matrigel tube-formation assay, and cell behavior in opposing media gradients was evaluated using a microfluidic chemotaxis device.

Results

DPSCs exhibited a potent neurogenic response, upregulating neuron-specific genes (e.g., NOS1, GRINs) and self-assembling into complex 3D neurospheres interconnected by bipolar-like cells expressing mature neuron markers, NF-M and βIII-Tubulin. Conversely, EGM induction did not drive endothelial differentiation. Instead, it primed DPSCs to adopt a pericyte-like phenotype, evidenced by the formation of rudimentary capillary-like networks on Matrigel.

Conclusion

Biobanked DPSCs demonstrate a unique, dual therapeutic potential. They successfully self-organize into pre-wired 3D neural networks and provide essential pericyte-like vascular support, positioning them as a superior candidate for regenerating the complex neurovascular architecture of the injured spinal cord.

Characterization of bone marrow mesenchymal stem cells from medication related osteonecrosis of the jaw patients

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Background
Osteonecrosis is a severe condition characterized by bone tissue necrosis resulting from impaired blood supply and disrupted bone remodeling. When occurring in the jaw and associated with antiresorptive or immunosuppressive medications, it is termed medication-related osteonecrosis of the jaw (MRONJ), a challenging disease with limited treatment options and significant impact on patient quality of life. Mesenchymal stem cells (MSCs) have shown regenerative potential in bone repair.
Therefore, this study aimed to evaluate the therapeutic potential of MSCs in MRONJ.

Methods
MSCs were isolated from 10 donors with MRONJ (hBMSC-MRONJ) and characterized in terms of morphology, colony formation, doubling time, viability, and multilineage differentiation capacity, then compared to MSCs from healthy donors (hBMSC-Healthy).

Results
Both MSC types adhered to tissue culture flasks, exhibited fibroblastic morphology, and formed colonies. hBMSC-MRONJ displayed a longer doubling time and lower viability over 7 days compared to hBMSC-Healthy. Osteogenic and adipogenic differentiation in both MSC types were confirmed by mineralized matrix formation and intracellular lipid vesicles, respectively. Immunophenotyping showed both MSC types were negative for CD34, CD45, and HLA-DR, and positive for CD73, CD90, and CD105, consistent with typical MSC markers.

Conclusions
MSCs derived from MRONJ patients retain key mesenchymal characteristics and multilineage differentiation potential, although with slightly reduced proliferation and viability compared to healthy MSCs. These findings suggest that MRONJ patient derived MSCs might hold potential as a therapeutic strategy for MRONJ, indicating a possible role in future regenerative treatment approaches.