ESM samples were isolated using an optimised acid decellularization protocol and the physical and mechanical characteristics assessed using DMA, SEM, WCA, FT-IR and TGA/DSC. In vitro biocompatibility and cytotoxicity were performed using fibroblast cell lines (i.e. Malme-3, Malme-3M and 3T3) and standard cell culture assays. Optimisation of PNIPAAm hydrogel and NP formulations were identified before being combined with the ESM. Thereafter, additional mechanical and physical characterisation including drug loading, release and diffusion were performed on this construct.

ESM samples were successfully prepared and fully characterized. Fibroblasts cultured on both the extracted ESM samples and ESM-gel demonstrated high biocompatibility in terms of high cell attachment, spreading, viability and proliferation rates. NP were successfully loaded into construct and demonstrated a desirable release profile depending on the specific formulation (days to weeks). As such, this work summarizes the development of an ESM-based construct that may have significant impact in regenerative medical applications.

Keywords: Eggshell membrane; Thermoresponsive; Skin

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DEVELOPMENT OF 3D CARDIAC MODELS VIA MAGNETIC MANIPULATION FOR DRUG SCREENING STUDIES

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Drug discovery and development process comprise of preclinical and clinical phases that are very intensive, long, and expensive research phases. However, drug candidates can fail in clinical trials. Toxicity is the major reason that leads to about 30% of drug development failures. Recently, the withdrawal rate of drugs from the market was increased to 33.3% from 5.1% due to cardiotoxicity. When the drug fails at phase I, the reasons are probably related to 2-dimensional (2D) cell culture studies that do not represent the real tissue physiology; therefore, they provide misdirected data about the efficacy and toxicity of drug. On the other hand, cells in 3D cell culture give responses more alike cells in vivo conditions in terms of cell morphology, growth, proliferation, migration, and drug sensitivity [1]. For that reason, 3D cell culture is a promising approach to overcome problems of conventional methods at the preclinical phase. To create 3D cell culture models, cell manipulation techniques have been used for various tissue-engineering applications. Contactless magnetic manipulation techniques provide rapid, simple, and cost-effective 3D cell culture model formation where either paramagnetic agent [2-5] or magnetic materials [6] were utilized. We have developed 3D cardiac model based on a contactless magnetic manipulation approach to investigate doxorubicin-induced cardiotoxicity. This technique provides an easy and efficient way to fabricate 3D cardiac cellular structures for drug screening studies compared to conventional methodologies.

Keywords: contactless magnetic manipulation; cardiac tissue engineering; drug screening

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Abstract 1891

GENOME WIDE TRANSCRIPTOME PROFILING ANALYSIS OF TRABECULAR MESHWORK PROGENITOR CELLS: THE FIRST STEP TO A CELL-BASED THERAPY TO RESTORE THE TRABECULAR MESHWORK IN GLAUCOMA

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Introduction: Loss and dysfunction of trabecular meshwork (TM) cells occurs with increasing age and is accelerated in primary open-angle glaucoma (POAG). TM progenitor cells (TMPCs) have the potential to repopulate the TM and could be used as a cellular therapy to restore the glaucomatous TM function. The biological properties and specific markers of TMPCs are still elusive. Understanding the transcriptome of TMPCs will identify specific markers and biological properties to facilitate the development of cell-based therapies to restore TM function in POAG.

Methods: Genome-wide transcriptome profiling was performed using RNA-seq of human primary TM cells (PTM), TMPCs and their differentiated cells (DTM) and analysed by using bioinformatics analyses. The differentially expressed genes (DEGs) of the three cell types were confirmed by NanoString.

Results: TMPCs proliferated, formed spheres, and could differentiate to TM cells in vitro. NanoString confirmed the RNA-Seq data and PLTP, PROS1, TIMP1 and MMP14 mRNA expression were increased in TMPCs compared with PTM cells. The IPA results identified that KDR, IGF1, FOS and MMP9 genes were nodal genes in the development of TMPCs. The activated pathways in the TMPCs which were related to the neuronal cell development.

Conclusion: TMPCs can be harvested and differentiated into the TM cells from human explant cultures in vitro. PLTP, PROS1, TIMP1 and MMP14 genes represent cellular markers for TMPCs. The pathways activated in TMPCs were consistent with the development of neuronal and endothelial cells. Understanding the key genes and pathways controlling TMPC biology are key to developing cell-based therapies for glaucoma.

Keywords: Glaucoma; Trabecular meshwork; Stem cell therapy

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BONE-TARGETING DELIVERY OF ALENDRONATE FOR THE TREATMENT OF OSTEOPOROSIS

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BACKGROUND & AIMS: Osteoporosis is a major health burden. Current therapeutic treatments have disadvantages such as systemic side effect and low bioavailability. Bone-targeting drug delivery system are designed to improve the therapeutic effect of drugs and minimize the potential toxic side effects. We fabricated a novel drug nanocarrier for bone-targeting alendronate delivery using glycol chitosan (GC)-poly(lactide-co-glycolide) (PLGA) and PLGA-alendronate conjugates.