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INTERACTION OF CHONDROCYTES WITH ELECTROSPUN POLYMER SCAFFOLDS DEPENDING ON THE FIBER ORIENTATION

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Objectives: Biocompatible polymer-based scaffolds with a tailorable degradation rate and a predefined structure might provide an approach to improve cartilage repair, which is limited by the poor intrinsic healing capacity of cartilage. The aim of this study was to explore whether electro-spin polymer scaffolds with different fiber orientation could influence the growth of primary articular chondrocytes.

Methods: Electro-spin scaffolds with aligned and random fiber orientation were prepared from two degradable polymers: poly(ethylene terephthalate urethane (PDG) and poly(glycol-dioxanone) (PDDO)) as well as polyethyleneimide (PEI) as a reference polymer, which is not intended to degrade. PDC was selected as a candidate material showing an almost linear mass loss in hydrolytic and enzymatic in vitro degradation experiments. Electro-spinning was conducted at ambient temperature using hexafluoro-2-propanol (HFIP) as solvent for PDG and PDDO, while PEI was processed from dimethylacetamide (DMAc) solution. The electro-spin structures exhibited an average deposition thickness of 80±50 μm with a single fibre diameter around 2-3 μm. Primary porcine articular chondrocytes were seeded on the ethylene oxides sterilized scaffolds and analyzed for viability, ultrastructure and type II collagen expression.

Results: Satisfactory numbers of vital chondrocytes could be detected on all electro-spin scaffolds, which were able to produce the cartilage-specific protein type II collagen. An flattened cell shape of the chondrocytes was observed on scaffolds with random fiber orientation, while on scaffolds with aligned fibers the chondrocytes exhibited a spherically cell shape and penetrated into the scaffold pores between the parallel fibers. Surprisingly, it was found that the chondrocytes did not align along the fiber direction.

Conclusions: Chondrocytes were able to grow on all polymer scaffolds tested and expressed the differentiation marker type II collagen. Cell morphology differed depending on the fiber orientation within the scaffolds.

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IONIC LIQUIDS IN NOVEL PROCESSING WAYS TO OBTAIN CHITOSAN- AND FIBROIN HYDROGELS FOR SKIN TISSUE ENGINEERING

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Objectives: The main goal of this work was to develop the application of green chemistry principles, namely the use of ionic liquids (ILs) and biorenewable sources, such as chitosan (CHT) and silk fibroin (SF), to newly process hydrogel-based constructs. The combination of this polysaccharide and protein may mimic the naturally occurring tissue environment. Although the solubilization of both materials in ILs has been studied individually, this work reports, for the first time, the use of ILs as a common solvent, for blending CHT/SF hydrogels production. These systems offer the advantage of being homogeneous and of presenting easy and short dissolution time of both biomacromolecules. Moreover, the intrinsic properties of these biopolymers are expected to accelerate the regeneration of chronic skin wounds.

Methods: Hydrogels were obtained by dissolving CHT and SF in 1-butyl-3-methylimidazolium acetate, [bmm][Ac] (4wt%) at different ratios. The systems were gelled and ILs removal was performed by Soxhlet extraction with ethanol. The effect of the chitosan source and CHT/SF ratio on consistency, crystallinity, protein adsorption and mechanical properties was evaluated. Moreover, the ability of the developed materials to support adhesion and proliferation of human dermal fibroblasts (hDFb) was assessed up to 21 days of culture.

Results: The findings suggest that [bmm][Ac] allowed the production of CHT/SF hydrogels with a soft end-to-end transition, good protein adsorption and viscoelastic behavior. Additionally, in vitro biological performance revealed a positive influence over adhesion, viability and proliferation of hDFb. Conclusions: The use of [bmm][Ac] as a common solvent provided a versatile approach to obtain CHT/SF hydrogels with interesting properties and with potential to sustain dermal fibroblasts outgrowth. This work constitutes a strong basis for future healing studies of chronic skin wounds.

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MICROBES BODELED FROM HUMAN ADULT MESENCHYMAL STEM CELLS PROTECT AGAINST ISCHEMIA-REPERFUSION-INDUCED ACUTE AND CHRONIC KIDNEY INJURY

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Objectives: Several studies demonstrated that mesenchymal stem cells (MSC) reverses acute kidney injury (AKI) in different experimental models by a paracrine mechanism rather than by MSC transdifferentiation. We recently demonstrated that microvesicles (MVs) released from MSCs may account for this paracrine mechanism by an horizontal transfer of mRNA and microRNA.

Methods: MVs were purified from MSC supernatants and were injected intravenously in rats (200μg/rat) immediately after monolateral nephrectomy and renal artery and vein occlusion for 45 minutes. To evaluate the MV effects on AKI induced by IRA, the animals were divided into different groups: normal rats (n=4), sham operated rats (n=6), IRA rats (n=8), IRA+MV (n=8), IRA+FNase (n=8) and all animals were sacrificed at day 2 after operation. To evaluate the CKD induced by IRA, the rats were divided into different groups: sham operated rats (n=6), IRA rats (n=8), IRA+MV (n=8) and all animals were sacrificed 6 months after the operation.

Results: We found that a single administration of MVs, immediately after injection of ischemia-reperfusion injury, protects rats from AKI by inhibiting apoptosis and stimulating tubular epithelial cell proliferation. The MVs also significantly reduced the impairment of renal function induced by ischemia reperfusion injury. Pre-treatment of MVs with FNase to inactivate their RNA cargo, abrogated these protective effects. Moreover, MPKI was also observed at 6 months in control rats with ischemia reperfusion injury.

Conclusions: MVs released from MSCs protect from ischemia reperfusion induced AKI and chronic renal injury, suggesting that MVs could be exploited as a potential new therapeutic approach.