Marine-derived collagen-based scaffolds support the proliferation and differentiation of human adipose derived stem cells envisaging cartilage regeneration.

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Cartilage lesions are very problematic due to the absence of self-regenerating capacity. Mimicking the physiological environment of its native tissue, promising tissue engineering approaches can be achieved to improve treatments efficiency.

Collagen-based materials offers advantages due to the presence of biochemical signals that support and induces cell attachment, migration and proliferation. Therefore, we propose with the present work the exploration of blue shark collagen to produce 3D structures envisioning cartilage tissue engineering applications.

Collagen was extracted from blue shark (*Prionace glauca)* skin using an optimized method and further solubilised in acidic conditions. After that, different concentrations of high molecular weight hyaluronic acid were added to the mixture, aiming to mimic the combination of proteins and glycosaminoglycans present in the extracellular matrix of cartilage. To increase scaffolds' stability, 3-4 hours of crosslink reaction with EDC at negative temperatures was allowed, further obtaining the desired scaffolds by freeze-drying.

As a first biological approach, *in vitro* cytocompatibility assays using human derived adipose stem cells (ASC) previously isolated from lipoaspirates were carried out. The blending and further crosslinking of both biopolymers resulted in cohesive hydrogels without the release of any harmful by-products. Metabolic activity assessment (MTS) confirmed the non-cytotoxic character of the different scaffold formulations. The produced structures support cell adhesion, migration and proliferation through the entire scaffold. The significant abundance of adhered cells one day after seeding was demonstrated by qualitative Live/Dead assay. Cell infiltration was observed by histological analysis using longitudinal sections of scaffolds stained with hematoxilin & eosin. In preliminary assays of hASC differentiation 14 days after cell seeding, SOX 9 expression was observed by immunohistochemistry on scaffold sections, suggesting the support of chondrogenic differentiation. As main conclusion, the proposed marine collagen:hyaluronic acid scaffolds revealed great potential to be applied as a tissue engineering approach to repair cartilage defects.

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