

## CELLULAR RESPONSE TO ANISOTROPIC FIBROUS/POROUS ELECTROSPUN SCAFFOLDS FOR CARTILAGE TISSUE ENGINEERING

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**Summary:** Tissue engineering (TE) strategies for repairing and regenerating articular cartilage face critical challenges to approximate the biochemical and biomechanical microenvironment of native tissues. The major challenge of TE cartilage is to mimic their mechanical properties to the native ones. The importance of the arcade-like collagen structure for the load-bearing properties in native cartilage is well emphasized in literature, but few studies have assessed the importance of collagen fibril depth-orientation on the mechanical properties of engineered-cartilage. To generate spatially-varying properties into TE-cartilage scaffolds, several combined cell-scaffold methods have been reported. Electrospinning allows the formation of arrays of aligned and random polymer-based nanofibers mats that can be assembled to mimic the structure of the native cartilaginous extracellular matrix. Mechanical stimulation can also be performed in order to create an anisotropic distribution of collagen in engineered-cartilage. Thus, a new series of anisotropic fibrous/porous electrospun scaffolds of polycaprolactone/collagen/graphene oxide were developed and their biocompatibility evaluated with and without mechanical stimulation using a bioreactor. First, anisotropic fibrous layers of PCL with depth-dependent variations in the fibrillar size and orientation were electrospun and then assembled and incorporated within a microporous graphene oxide/collagen structure. Several architectures were produced and tested in vitro. For this, a cartilage progenitor cell line was used and the cell metabolic activity, morphology and distribution throughout the scaffolds were accessed. The results, both static and dynamic, revealed that the scaffolds could not only allow cells' adhesion, but also cell proliferation. Overall, polycaprolactone/collagen/graphene oxide scaffolds generated a good cellular response and were able to support cell proliferation. The effect of mechanical stimulation under physiological conditions is discussed. This work was supported by the funding of Program COMPETE-FEDER, Programa Operacional Competitividade e Internacionalização through the project POCI-01-0145-FEDER-016574 and by Fundação para a Ciência e Tecnologia I.P. (FCT, IP) through the project PTDC/EMS-TEC/3263/2014. The authors thank to FCT for the PhD grants SFRH/BD/133129/2017 and SFRH/BD/130287/2017.