Injectable Microscaffolds for IVD Regeneration

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INTRODUCTION: Injectable biomaterials for drug and cell delivery into the degenerated intervertebral disc are of high clinical need. Here we report on the fabrication of ECM-like, injectable nanofibrous microscaffolds (MS). The MS were cultured with Mesenchymal Stem Cells (MSC) and Nucleus Pulposus cells (NPC) and their injectability was tested with the use of 23-26G needles.

METHODS: PLLA, PLGA and PCL nano- and microfibers were electrospun on glass collectors and then structured into microscaffolds with a picosecond laser. MS were functionalised with natural polymers: chitosan and chondroitin sulfate. We used Scanning Electron Microscopy (SEM) for morphological characterisation of MS with and without cells. NPC and MSC cells were used to assess the biocompatibility of produced MS and the possibility to inject them as a biomaterial-cell construct. In vivo study in the pig model of intervertebral disc degeneration was conducted to assess the safety and potential of MSC-laden MS in IVD regeneration.

RESULTS: With the use of biomaterials of high porosity, cell-protective MS can be formed which could lead to an increase in the survival rate of injected cells. Any shape of microscaffolds can be created when using laser processing, as shown in Fig. 1a. However, the cube-like shape is preferential due to low structurization time. The cytocompatibility assays show an increase in cell number with culture time. The MSC cells attached well to the fibres (Fig. 1b,c) and populated MS at each side, resulting in the formation of MS agglomerates. The injectability studies through 26G and 24G needles showed that the ejection rate was 92% and 97%, respectively. In the in vivo study, after nucleus pulposus vaporization, MSC-laden MS labelled with superparamagnetic iron oxide nanoparticles were injected into the tissue. Suitable deposition of the construct was observed without leaking through the needle path.

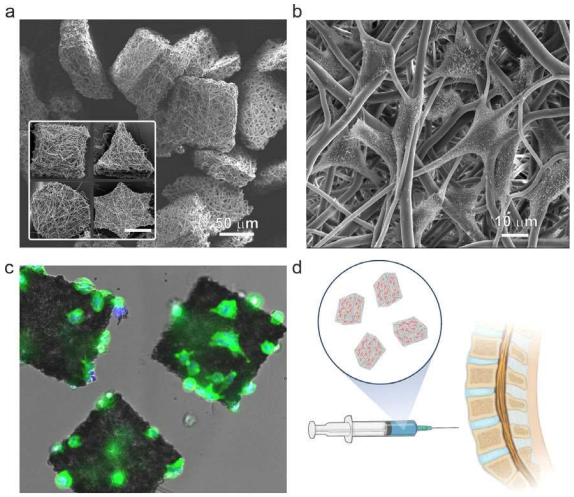

Fig. 1: MS fabrication and biocompatibility a) SEM micrograph presenting cut MS b) MSC cells spreading filopodia between fibres c) morphology of NPC cells on the MS's surface d) scheme presenting proposed use of the cell-laden microscaffolds.

DISCUSSION & CONCLUSIONS: MSs are compatible with living tissues and readily populated with cells. By functionalising the surface of nanofibers, the physical and chemical structure of MSs can be customised to improve cell-MS interaction. The surface modification could provide additional functionality like neuroinhibitory properties with the use of chondroitin sulfate. The injectability studies show that polymer-based MSs are injectable through the tested range of needle sizes and improve disc height when minimally invasively injected into degenerated IVD.

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