Stage Master 2
Development of biomimetic tools for cartilage tissue engineering

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Scientific project :

Objectives

This project aims to develop biomaterials able to host mesenchymal stem cells (CSMs) et induce their differentiation into chondrocytes for cartilage tissue engineering. Our objective is to produce an engineered tissue *in vitro* that replicates the biological and mechanical properties of native cartilage for future applications in regenerative medicine. Our approach consists in targeting receptors expressed on the surface of MSCs that induce chondrogenesis, using biomimetic peptides. In particular, we are interested in the α10β1 integrin, a collagen-binding receptor which plays a key role in extracellular matrix (ECM) production and cartilage homeostasis.

Approach

Biomaterials will be produced as hydrogels (from PEG or alginate) functionalized with ligands for collagen-binding receptors, in particular α10β1, which have recently been discovered in our laboratory. These ligands are triple-helical peptides (THPs), a family of peptides that adopt the characteristic triple helix structure of collagen. In this 3D culture system, CSMs encapsulated in hydrogels will be differentiated in chondrocytes in the presence of growth factors et mechanical stimulation. CSM/biomaterial interactions will be provided by THP recognition by collagen-binding receptors, thus mimicking natural interactions between cells and the ECM. CSM differentiation will be monitored by immunofluorescence and PCR, probing for transcription factors or markers for chondrocytes (*SOX9*, *ACAN*, *COL2* et *COL9*) or other lineages (for instance *Osx*, *Runx2*, *COL1*, *COL10* for osteocytes or hypertrophic chondrocytes). We will also explore α10β1 integrin activation and associated signalling pathways (MAP kinase phosphorylation, actin polymerisation, formation of focal adhesion points). Finally, we will study the ability of differentiated CSMs to produce ECM corresponding to that of cartilage, by analysing both its composition (by immunofluorescence, western blot and mass spectrometry) and its bio-mechanical properties (by measuring rigidity and elasticity of engineered cartilage tissues obtained in the presence of mechanical constraints similar to those found in joints of the hip or the knee).

Publications:

- **J.-D. Malcor**, F. Mallein-Gerin, *Biomaterial functionalization with triple-helical peptides for tissue engineering*, Acta Biomaterialia 148 (2022) 1-21.
- **J.-D. Malcor**, D. Bax, S.W. Hamaia, N. Davidenko, S. Best, R. Cameron, R. Farndale, D. Bihan, *The synthesis and coupling of photoreactive collagen-based peptides to restore integrin reactivity to an inert substrate, chemically-crosslinked collagen*, Biomaterials 85 (2016) 65-77.
- **J.-D. Malcor**, E. Hunter, N. Davidenko, B. Bax, S. Best, R. Cameron, S. Sinha, R. Farndale, *Collagen scaffolds functionalized with triple-helical peptides support 3D HUVEC culture*, Regenerative Biomaterials 5 (2020) *7* 471-481.