

Master Internship offer

Date of the offer: 23th of July 2020

Internship supervisor and Host laboratory:

- *Lab*: Laboratoire de biologie Tissulaire et Ingénierie thérapeutique (LBTi – CNRS UMR 5305)
- *Group* : « Biologie et Ingénierie du Cartilage »
- *Team leader*: Dr Frédéric Mallein-Gerin, Research director, f.mallein-gerin@ibcp.fr, 04 37 65 29 19
- *Supervisor for the internship*: Dr Emeline Perrier-Groult, emeline.groult@ibcp.fr, 04 72 72 26 17)
- *Address of the internship*: IBCP, 7 passage du Vercors, 69007 Lyon
- *Team Website*: <https://lbtibcp.fr/>
- *Languages spoken in the lab*: French / English

Research project title:

Role of $\alpha 10\beta 1$ integrin in chondrocyte mechanotransduction

Keywords : Chondrocytes, Cartilage, Mechanotransduction, Integrin, signaling pathways

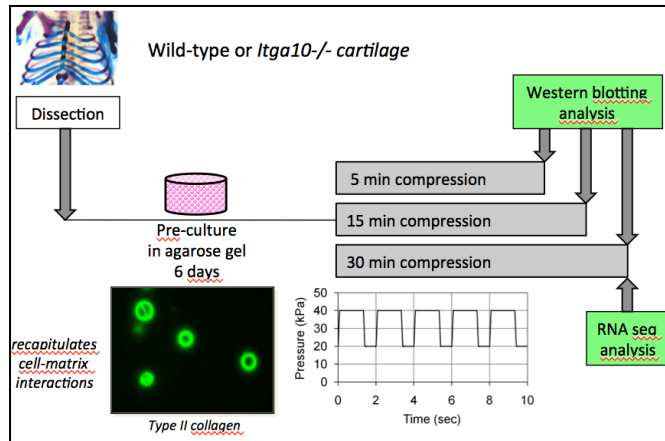
Description du projet / Project description (subject and technics):

Context:

Although osteoarthritis (OA) can be initiated by multiple factors at multiple sites, mechanical overloading remains a key feature of OA pathogenesis. OA may result from excessively aberrant or physiologically normal mechanical stresses on initially healthy or pathologically-impaired articular cartilage, bone and ligaments. There is thus a need to decipher the mechanotransduction pathways involved in these tissues since alterations in these pathways likely increase the risk of OA. Our project focuses on the mechanotransduction in cartilage. Chondrocytes exposed to mechanical forces transmit the signals via various mechanotransducers including stretch-activated ion channels, receptor tyrosine kinases, the hyaluronan receptor CD44 and integrins. Integrins are transmembrane proteins consisting of α and β subunits and almost all cartilage proteins bind to integrins. Chondrocytes primarily use $\beta 1$ integrins for adhesion to the cartilage matrix but the participation of the individual $\beta 1$ integrin heterodimers in articular cartilage mechanotransduction is not clearly defined. While most literature data propose the fibronectin receptor $\alpha 5\beta 1$ integrin as a critical mechanotransducer, the role of the prominent collagen-binding integrins such as $\alpha 10\beta 1$ is unknown. The prominent expression of $\alpha 10\beta 1$ integrin in articular chondrocytes and the partially overlapping chondrodysplasia phenotype of *Itga10* null mice and mice with cartilage-specific deletion of *Itgb1* makes us think that $\alpha 10\beta 1$ is an integrin heterodimer which plays pivotal roles for functional and mechanical integrity of the joint tissue.

Internship project:

Our specific objective is to determine the role of $\alpha 10\beta 1$ in chondrocytes mechanotransduction. We will use a cell system consisting of wild-type or *Itga10* null chondrocytes embedded within agarose hydrogels and submitted to compression. We will investigate the impact of $\alpha 10$ privation on the phosphorylation state of signaling molecules and transcriptome (RT-qPCR, Western-blotting, Immunofluorescence). This project will bring new insight into how chondrocytes respond to mechanical forces, under the control of $\alpha 10\beta 1$ integrin.



Workflow of the analysis of the effect of compression on gene expression and activation of signaling molecules in presence or absence of $\alpha 10$ integrin.

Lab publications or recommended review on the subject:

- 1- CUERU L, BOUGAULT C, ASZODI A, BERTHIER Y, MALLEIN-GERIN F, SFARGHIU AM. Mechanical and physicochemical responses for hyaline cartilage: role of protein $\beta 1$ integrin in mechanotransduction. *Comput Methods Biomech Biomed Engin.* 2013;16 Suppl 1:330-1.
- 2- BOUGAULT C, CUERU L, BARILLER J, MALBOUYRES M, PAUMIER A, ASZODI A, BERTHIER Y, MALLEIN-GERIN F, TRUNFIO-SFARGHIU AM. Alteration of cartilage mechanical properties in absence of $\beta 1$ integrins revealed by rheometry and FRAP analyses. *J Biomech.* 2013 Jun 21;46(10):1633-40.
- 3- BOUGAULT C, AUBERT-FOUCHER E, PAUMIER A, PERRIER-GROULT E, HUOT L, HOT D, DUTERQUE-COQUILLAUD M, MALLEIN-GERIN F. Dynamic compression of chondrocyte-agarose constructs reveals new candidate mechanosensitive genes. *PLoS One.* 2012;7(5):e36964.
- 4- GOUTTENOIRE J, BOUGAULT C, AUBERT-FOUCHER E, PERRIER E, RONZIÈRE MC, SANDELL L, LUNDGREN-AKERLUND E, MALLEIN-GERIN F. BMP-2 and TGF-beta1 differentially control expression of type II procollagen and alpha 10 and alpha 11 integrins in mouse chondrocytes. *Eur J Cell Biol.* 2010 Apr;89(4):307-14.
- 5- BOUGAULT C, PAUMIER A, AUBERT-FOUCHER E, MALLEIN-GERIN F. Investigating conversion of mechanical force into biochemical signaling in three-dimensional chondrocyte cultures. *Nat Protoc.* 2009;4(6):928-38.