

DOC POSITION ANNOUNCEMENT – Osteoimmunology

A doc position will be available at St-Etienne University, on the topic: “Effect of mechanical stresses on YAP/TAZ activation and on bone loss and subchondral bone damage in arthritis”.

This **PhD position** is located at Medicine Faculty, SAINBIOSE INSERM U1059 (St-Etienne University led by L Vico) in the team “Integrative Biology of the Bone Tissue”. The position will be funded by the French Research Minister and will support research led by Hubert Marotte, who will lead the team “Integrative Biology of the Bone Tissue” from SAINBIOSE Univt. The work will be also performed in collaboration with a variety of colleagues across the team. The position is for three years.

Topic: Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatic disease responsible for joint destruction, i.e. erosion. The practice of adapted physical activity is increasingly recommended in chronic diseases. The joint is composed of the synovial membrane and cartilage covering the subchondral bone tissue. We have already shown that bone loss preceded arthritis with the kinetic involvement of the different actors of the Wnt pathway. In addition, we have demonstrated the impact of YAP/TAZ, a family of mechanotransducers, on arthritis-related joint damage. The synoviocyte got a specific phenotype during RA and YAP appeared to be the mediator involved in this phenotype in response to an increase in pressure localized in the joint. In addition, inhibition of YAP decreases this hypertrophy and helps to regulate the inflammatory response and decrease joint damage in an arthritis model (Paper in Revision). Hyperactivation of YAP/TAZ via physical activity could therefore be deleterious with increased joint destruction. So, it is critical to check the clinical phenotype of arthritis, the expression of YAP/TAZ and the analysis of joint damage during arthritis subjected to different mechanical stresses:

- an increase in mechanical stress via i/ physical activity during the pre-clinical phase of arthritis or ii/ an increase in severity (centrifuge)
- a reduction in the mechanical stress on the rear axle by tail suspension.

In parallel, an analysis of the expression of YAP/TAZ in our organoid model subjected to mechanical stresses by the bioreactor and a characterization of the YAP regulation zones will be performed using the mass spectrometry of the DVH team (second team of SAINBIOSE Unit).

The **applicant** will work on primary cells, transfected cells and in rat arthritis model. A large panel of technical tools will be used from cell culture to western blots and mass spectrometry analysis for the in vitro works. In parallel, in vivo study with rats will be done including arthritis development in various conditions of mechanical stress. The applicant must hold a Master degree in a relevant discipline. She or he will be invited in the editing of at least two publications and will have the opportunity to participate to at least one international meeting.

Please **send** a cover letter indicating your motivation and experience, a brief (2 page) description of your research interests, your CV, a graduate transcript, and list of peer-reviewed publications. Please arrange to have two to three confidential letters of recommendation.

Documents will be sent to hubert.marotte@inserm.fr