

MARIE SKLODOWSKA-CURIE ACTIONS

Co-funding of regional, national and international programmes (COFUND)

DOC2AMU THESIS PROJECT 2018 CALL FOR APPLICATIONS

Smart interrogation of mechanosensing in T cell activation

Biological linkers, in the form of ligand-receptor bonds, are mechanosensitive structures since their kinetics and strength are force dependent. Living cells too are mechanosensitive, at a different scale - their structure and function depend on forces that they sense and exert. However, a big current challenge, and the overarching goal of this project, is to bridge our understanding of the molecular and cellular scales, in space and time. Here, we shall focus on the T cell immune response, which is at the heart of our acquired immunity. We set to design innovative substrates to manipulate adhesion using state-of-art micro and nano-fabrication techniques while measuring cell generated forces and develop the means to couple cell force measurements with atomic force microscopy (AFM) and optical tweezers (OT) in order to simultaneously record modulation of cell mechanics and forces. We shall also quantify cellular activation levels which will be linked to theoretical models derived from our current work. In brief, we aim to **describe mechanotransduction from molecular to cellular level in the frame of T cell activation.**

Supervisors and Host Laboratories: The project will be carried out jointly in two laboratories in Marseille. France: the Adhesion and Inflammation Laboratory (LAI), which specialises in biophysics of the immune system, and the interdisciplinary center for nano-sciences (CINaM), which specialises in nano-materials including in the context of cell biology. At LAI, the thesis will be supervised by **Pierre-Henri Puech** who dissects mechanosensing at single cell scale by a combining high resolution surface optical microscopy and force based techniques such as AFM and OT. Expertise in T cell biology and genetic manipulation is available at LAI. Close collaboration with **Laurent Limozin** (LAI) is planned for analysis of advanced microscopy data and modelling. At CINaM, the thesis will be supervised by **Kheya Sengupta** who focuses on adhesion of living cells and cell models, *via in-vitro* experiments using cell mimetic systems, including those designed to probe the dynamics and spatial organization associated with inter-cellular adhesion in general and the immunological synapse in particular.

Interdisciplinary and intersectoriality: Mechanobiology has fascinated biologists and physicists alike for more than a decade. This highly interdisciplinary project integrates techniques and concepts from surface chemistry, micro-engineering, cell biology, and cell bio-physics. The company JPK Instruments (Berlin, Germany), which builds AFMs and OTs and is a long term collaborator of LAI, will contribute towards development and training. The LFO FabLab / Resonance situated at La Friche Belle de Mai (Marseille) will help in designing and building, at low costs and hi versatily, the small equipments that the experiments may require.

The candidate: The candidate must have must have a basic bachelor level degree in physical sciences or engineering, and a master degree in physical or biological sciences. (S)he will do experiments, which will include substrate preparation, cell manipulation and optical/atomic-force microscopy, as well as extensive data analysis. Preference will be given to candidates with prior experience in cell culture/manipulation, advanced optical microscopy, and/or force based biophysical techniques. Prior training in computer programming and basic mathematics is desirable but not essential – however willingness to learn these skills is a must.

About DOC2AMU: DOC2AMU is a special PhD call from the Aix-Marseille University, in collaboration with the EU. The PhD is funded for three years. Dedicated funding for the travel of the student as well as for costs associated with the project is provided within the grant. The student will be expected to spend part of their research time abroad, in the framework of collaborations, and also be trained in the private sector. Please contact either P-H. Puech (pierre-henri.puech@inserm.fr ; <https://phpuech.wordpress.com/>) or K. Sengupta (sengupta@cinam.univ-mrs.fr ; <http://www.cinam.univ-mrs.fr/cinam/spip.php?page=perso&name=sengupta>) with your CV and a letter of motivation. The application will be screened and the selected applicant will be presented to Doc2AMU for further selection. About 50% of the projects are expected to be funded. More information is available at: <https://doc2amu.univ-amu.fr/en>