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ICFO
The Institute
of Photonic
Sciences



Master in Photonics – “PHOTONICS BCN” Master ERASMUS Mundus “EuroPhotonics”

MASTER THESIS PROPOSAL

Dates: April 2021 - September 2022

Laboratory: Single Molecule Biophotonics

Institution: ICFO-Institut de Ciències Fotoniques

City, Country: Castelldefels, Barcelona, Spain

Title of the master thesis: Assessing the role of mechanical forces on immune integrin receptors by single molecule imaging methods

Name of the master thesis supervisor and co-supervisor: Maria Garcia-Parajo

(for external proposals a co-supervisor from the Master program is needed)

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Keywords: Mechanical forces, integrin activation, time-lapse single particle tracking, leukocyte adhesion cascade

Summary of the subject (maximum 1 page):

Mechanical cues have long been overlooked as key players in the signaling pathways of cells. Whereas biochemical signals have been predominantly studied in the context of the immune system, more recent studies are pointing to mechanical stimuli as additional and important players regulating signaling pathways and providing means for cells to sense their environment. It has been recently shown by our group and others that the nanoscale spatiotemporal organization of molecules inside living cells plays an important role in cell function but the role of mechanical forces regulating this dynamic nanoscale spatial organization has not been addressed yet.

The goal of this research project is to investigate the role of mechanical forces in the activation and spatiotemporal organization of a key cell adhesion receptor common to most immune cells: the integrin LFA-1 (also called $\alpha_L\beta_2$). This integrin is involved in the initiation of processes such as the formation of the immunological synapse, leukocyte adhesion and its transendothelial migration (TEM) from the blood vessels. LFA-1 is a transmembrane protein



with a nanoscale architecture expected to be highly relevant to its function and highly sensitive to mechanical stimuli. The project will address the effect of mechanical stimuli on the nanoscale organization of LFA-1 and its conformational states. We will use immune cells (different kinds of leukocytes) to look into the effect of different shear flow conditions on LFA-1 with a combination of methods particular to our lab. The project will use different approaches such as microscopy-compatible shear flow devices combined with multi-colour single particle tracking (SPT). If time is available, the student will also be exposed and perform super-resolution microscopy of LFA-1 on fixed T cells after shear-flow stimulation.

Specific tasks to be performed by the student

1. Study the literature in the field, which is very abundant but also extremely controversial.
2. Incorporation of DIC imaging and synchronization electronics on a multi-colour SPT: this imaging methodology will enable interleaved cell imaging together with multi-colour SPT and all temporally synchronized by the sCMOS camera.
3. Get familiar with the acquisition of SPT data and its evaluation, followed by the proper data interpretation.
4. Perform interleaved DIC measurements on leukocyte phenotype and cell migration speed together with SPT on leukocytes in the presence of shear-flow.
5. SPT analysis correlated with cell phenotype and migration state as function of shear-flow.

Additional information (if needed):

* Required skills : No prior knowledge or experience in biology is required, but the candidates are expected to be keen on understanding cell biological processes and learning new techniques.

* Miscellaneous :