

PhD GRANTS 2021

PhD project title: Rewiring programmed cell death and Inflammation via Modulation of ERK signalling Dynamics (RIMED)

PhD Supervisor: Franck Riquet

Co-supervisor(s): Benjamin Pfeuty

Laboratory: PhLAM

Research program(s) concerned (CPER, Labex/Equipex, ANR, Europe, LAI ...):

Cotutelle (Y/N): N

Any other relevant information:

Application procedure & Eligibility criteria :The application procedure and eligibility criteria are detailed on the European doctoral programme PEARL website www.pearl-phd-lille.eu. The funding is managed by the I-SITE ULNE foundation which is a partnership foundation between the University of Lille, Engineering schools, research organisms, the Institut Pasteur de Lille and the University hospital.

The application file will have to be submitted before March 31, 2021 (10:00 AM - Paris Time) and emailed to the following address : international@isite-ulne.fr.

Net salary and Lump Sum: A net salary of about €1,600 + €530 per month to cover mobility, travel and family costs.

PhD project summary:

Cellular stress can promote responses *via* the activation of signalling pathways ranging from survival to eliciting the initiation of programmed cell deaths (PCDs) such as necroptosis and apoptosis. While necroptosis is more inflammatory, due to the release of cytokines, chemokines and damage-associated molecular patterns, apoptosis is considered as a less immunogenic cell death modality. A main challenge in this context is to identify modulators that can dampen the immunogenic signature associated with PCDs and especially in necroptosis conditions.

Our recent findings and that of others show that ERK is involved in necroptosis-activated cell autonomous functions *via* the increase of pro-inflammatory cytokines gene expression. Using quantitative ERK signalling dynamics analysis via biosensor imaging, we revealed distinct amplitude- and frequency-modulated (AM/FM) ERK activity signalling dynamics in L929 depending on the triggered cellular process: survival, apoptosis, or necroptosis. We propose that (AM/FM) ERK signalling dynamics would mediate proinflammatory cytokine gene expression increase during TNF-induced necroptosis in L929.

To test this hypothesis, we need to establish the causality link by investigating the origin of ERK signalling dynamics (pulse generator) and the correlation between ERK signalling dynamics and pro-inflammatory gene expression patterns at the single cell level during necroptosis. An important goal is the implementation of combined biosensing imaging with layered immunofluorescence at the single cell level for correlation purposes. This unique project is meshing cellular and molecular biologists, theoretical physicist, live cell imaging and compound screening specialists, and computer scientists (machine learning for data analysis and processing) around a fully functional biosensing pipeline that will be transversally coupled to modelling approaches and multiplex screening assay context (*planned secondments with Coll. D. Audernaert Screening Core/C-BIOS-VIB/UGhent Belgium & H. Fearnhead ARC National University of Ireland Galway*).