

Title of the thesis	Rewiring programmed cell death and Inflammation via Modulation of ERK signalling Dynamics
Acronym	RIMED
Reference number	021

Hosting institution	Employer
Université de Lille Website: https://www.univ-lille.fr/home/	CNRS Website: https://www.hauts-de-france.cnrs.fr/fr/delegation
Hosting research unit 1	Hosting research unit 2
<u>Name:</u> laboratoire de Physique des Lasers, Atomes et Molécules <u>Acronym:</u> PhLAM <u>Identification number:</u> UMR 8523 <u>Address:</u> Building P5 campus Cité Scientifique 2 Avenue Jean Perrin 59655 Villeneuve d'Ascq cedex Website: https://phlam.univ-lille.fr/en/	<u>Name:</u> laboratoire de Physique des Lasers, Atomes et Molécules <u>Acronym:</u> PhLAM <u>Identification number:</u> UMR 8523 <u>Address:</u> Building P5 campus Cité Scientifique 2 Avenue Jean Perrin 59655 Villeneuve d'Ascq cedex Website: https://phlam.univ-lille.fr/en/
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Thesis information	
Keywords	ERK, Signaling dynamics, Immunogenic Cell Deaths, Modelisation, HCS
Abstract	<p>Cellular stress can promote responses <i>via</i> 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.</p> <p>Our recent findings and that of others show that ERK is involved in necroptosis-activated cell autonomous functions <i>via</i> 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.</p> <p>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,</p>

	<p>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 (<i>planned secondments with Coll. D. Audernaert CSF VIB VIB Ghent Belgium & H. Fearnhead ARC NUI Galway</i>).</p>
Expected profile of the candidate	<p>Funded by the doctoral programme Pearl coordinated by the Foundation I-SITE ULNE, we are looking for ambitious PhD students with interest in quantitative single cell biology and high content screening (HCS) approaches within a consortium made of four labs with complementary expertise. The multidisciplinary RIMED project will investigate the Rewiring programmed cell death and Inflammation via Modulation of ERK signalling Dynamics as potential therapeutic approach to dampen immunogenic consequences in necroptosis-associated conditions.</p> <p>Candidates with a Degree in Biology, Biochemistry, Bioengineering, Biophysics or a closely related field should apply. Experience with molecular biology, cell culture, live cell imaging and programming are advantages, but are not an absolute requirement. The students are expected to interact within a multidisciplinary environment and to closely collaborate with all members of the consortium. Spoken and written English are required.</p>
Application procedure & Eligibility criteria	<p>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.</p> <p>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.</p>
Net salary and Lump Sum	<p>A net salary of about €1,600 + €530 per month to cover mobility, travel and family costs.</p>