Université de Lille

PhLAM

cnrs

CONTRACTS DOCTORAUX 2023

Titre du projet de thèse :

Decoding ERK necroptotic signaling dynamics via live RNA detection of cytokine gene expression (NecroCytoCode)

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Résumé du projet de thèse (en 20 lignes maximum) :

Background and context: Cellular stress can promote responses via the activation of signaling pathways ranging from survival to eliciting the initiation of regulated cell deaths (RCDs) 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.
State of the art and hypothesis: It is now recognized that cells encode information based on the temporal modulation of signaling activities aka signaling dynamics. 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 signaling dynamics analysis via biosensor imaging, we revealed distinct amplitude- and frequency-modulated (AM/FM) ERK activity signaling dynamics in L929 depending on the triggered cellular process: survival, apoptosis, or necroptosis. We propose that (AM/FM) ERK signaling dynamics would mediate proinflammatory cytokine gene expression increase during TNF-induced necroptosis in L929. A main challenge in this context, and in the field at large, is to establish the correlation between ERK signaling dynamics and pro-inflammatory gene expression patterns at the single cell level during necroptosis.
Aim and research objective: Thus an important goal is the implementation of combined biosensing imaging with live RNA detection at the single cell level for correlation purposes. This unique project is meshing cellular and molecular biologists, theoretical physicist, live cell imaging around a fully functional biosensing pipeline that will be transversally coupled to modelling approaches.
Relevance: This research project proposes to tackle the next essential step in signaling dynamics critical to better understand physiological and pathological situations in which signaling pathways are being rewired, resulting in changed signaling dynamics of molecular effectors (encoding) affecting cytokine gene expression pattern (decoding), all together leading to cellular re-programming.