

Supervisor(s):

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Host laboratory:

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Host group/team:

Gen&Chem

Title of the M2 research internship:

Intracellular calcium signalling in cancer cells

Project summary:

Calcium ions (Ca²⁺) are vital cations that influence practically every aspect of cellular functions. Intracellular Ca²⁺ signalling is critical in cell proliferation, migration and cell death and a dysregulation of Ca²⁺ homeostasis can have detrimental effects on cell health and survival. A growing body of evidence points to a functional link between impairment in cellular Ca²⁺ homeostasis and cancer pathogenesis. Recent studies have shown that cancer cells exhibit spontaneous intracellular Ca²⁺ transients. These Ca²⁺ oscillations control downstream intracellular signalling cascades that regulate the proliferation of cells and the growth of tumours. The mechanisms sustaining the spontaneous elevations of intracellular Ca²⁺ in cancer cells are still poorly understood. Given the pathophysiological importance of cellular Ca²⁺ signalling, it is crucial to fully understand these Ca²⁺ responses of cancer cells.

Ubiquitination consists in the attachment of ubiquitin (Ub) to target proteins. This reversible post-translational modification controls various key cellular processes like the localization, activity, trafficking, endocytosis, and degradation of proteins. Deregulation of the Ub conjugation/deconjugation system is associated to the pathogenesis of various diseases particularly cancer and inflammatory diseases. The interplay between Ca²⁺ signalling and the Ub system is virtually not documented. We have recently revealed the involvement of the DUB UCHL1 in the control of the cellular Ca²⁺ signalling. This is of particular relevance because UCHL1 has been identified as an oncogenic DUB notably in prostate cancer. Moreover, its inhibition exerts anticancer effects (Cell Reports Medicine, 2024, 5:101381). We plan to characterize the role of UCHL1 in prostate cancer cells with a focus on transmembrane Ca²⁺ transport systems. This project will provide new insights into the pathophysiological functions of UCHL1 and pave the way to a better understanding of its tumorigenic functions.

Understanding the roles of DUBs in cellular Ca²⁺ signalling is a new project launched in the lab these past few years. Originally, the project was dedicated to the understanding of the roles played by DUBs in neuronal functions with a strong emphasis on n

Keywords:

cancer, intracellular signalling, ubiquitination

Relevant publications of the team:

- Bouron A (2023) Neuronal store-operated calcium channels, *Molec Neurobiol*, 60: 4517-4546.
- Bouron A, Aubry L, Loreth D, Fauvarque MO, Meyer-Schwesinger C (2023) Role of the deubiquitinating enzyme UCHL1 in mitochondrial function, *Front. Cell. Neurosci*, 17:1149954.
- Bouron A (2022). Store-operated ion channels: a growing family ? *Cell Calcium*, 107:102657.
- Bouron A, Fauvarque MO (2022). Genome-wide analysis of genes encoding core components of the ubiquitin system during cerebral cortex development. *Molec Brain*, 15: 72.
- Bouron A (2020). Transcriptomic profiling of Ca²⁺ transport systems during the formation of the cerebral cortex in mice. *Cells*, 9:1800.