Grenoble Alliance for Integrated Structural & Cell Biology

GRAL MSc RESEARCH SCHOLARSHIP 2020-2021

RESEARCH INTERNSHIP PROPOSAL

Institute / Group

IRIG / BGE – Gen&Chem

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Research Project Title

Investigating an epigenetic pathway in a deadly emerging fungal superbug

Description of the project

Cell response to external signals is dependent on cell surface receptors that are tightly controlled by endocytosis. Their trafficking to lysosomes relies in part on the ESCRT-III complex. This flexible multi-subunit machinery is able to form spiral polymers and to drive a topologically unique membrane deformation and scission event, required for the biogenesis of intraluminal vesicles in endocytic compartments, cytokinesis, autophagic vesicle formation and budding of viruses such as HIV. This project proposes to dissect the role of an atypical member of the ESCRT III protein family, the protein CHMP1B. We will (1) characterize the CHMP1B polymers and tubules induced by the protein overexpression in HeLa cells by electron and confocal microscopy approaches (anchoring sites, presence of known partners and membrane markers in the polymers/tubules…), (2) explore the contribution of lipids to CHMP1B recruitment to specific membranes using purified recombinant human CHMP1B and in vitro assays, and (3) investigate the role of CHMP1B ubiquitination by the ubiquitin-specific protease USP8 in polymer formation using molecular/cellular approaches. This will provide a deeper understanding of CHMP1B regulation by USP8 whose uncontrolled expression is associated with Cushing's disease and chemoresistance in lung cancers.

The recommended background for the candidate is cell biology and biochemistry, and knowledge in cell signalling.

Keywords

ESCRT machinery, polymerization, membrane remodelling, ubiquitination

Relevant publications of the team

CHMP1B is a target of USP8/UBPY regulated by ubiquitin during endocytosis. Crespo-Yàñez X, Aguilar-Gurrieri C, Jacomin AC, Journet A, Mortier M, Taillebourg E, Soleilhac E, Weissenhorn W, Fauvarque MO. PLoS Genet. 2018, 14(6).

Calcium influx mediates the chemoattractant-induced translocation of the arrestin-related protein AdcC in Dictyostelium. Mas L, Cieren A, Delphin C, Journet A, Aubry L. J Cell Sci. 2018, 131(19).

Dictyostelium Tom1 participates to an ancestral ESCRT-0 complex. Blanc C, Charette SJ, Mattei S, Aubry L, Smith EW, Cosson P, Letourneur F. Traffic. 2009, 10(2).