« PROPOSITION DE STAGE M2 »

Laboratoire : Physico Chimie Curie Institut Curie UMR 168

Adresse : Institut Curie, 11 rue P. M. Curie 75005 Paris

Directeur du laboratoire : Pascal Hersen

Équipe de recherche (si pertinent) : Molecular Microscopy of Membranes

Responsable de l'équipe : D. Lévy

Responsable de stage : D. Lévy

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N° et intitulé de l'Ecole Doctorale de rattachement : ED515 Complexité du Vivant

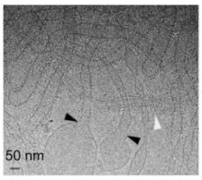
Profil recherché : biophysic, biochemistry, computational analysis.

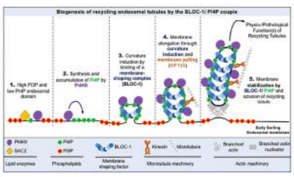
Possibilité de poursuite en thèse : possible

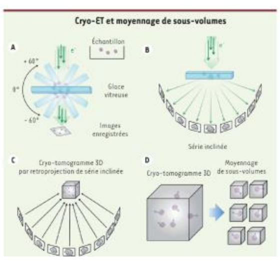
Si oui financement envisagé : ED 515, PSL, ANR

Titre du stage: 3D architecture at sub-nanometric resolution of BLOC-1 endosomal complex by cryo-electron microscopy

Abstract : Intracellular trafficking is mediated by transport carriers that originate by membrane remodeling from donor organelles. Tubular carriers play major roles in the flux of membrane lipids and proteins to acceptor organelles. We have shown by cryo-electron microscopy that phosphatidylinositol-4-phosphate (PI4P) and biogenesis of lysosome-related organelles complex 1 (BLOC-1) govern the formation, stability and functions of recycling endosomal tubules (1). RE malfunction is associated with diseases such as neurological disorders (e.g., Huntington and Alzheimer diseases) or genetic forms of oculocutaneous albinism. A central question is how a phospholipid and a protein complex coordinate as a minimal machinery to remodel cellular membranes into functional tubes. Thanks to state-of-the-art cryo-electron tomography and advanced images analysis, it is now possible to address this question at the molecular scale (2, 3).
The goal of the internship will be built 3D architecture of BLOC-1 at sub-nanometric resolution by cryo-electron tomography and images analysis (3).
The student will be trained in the membrane biochemistry, cryo-electron microscopy and image analysis with the help of biochemists and cryo-electron microscopists in the Molecular Microscopy of Membranes team in Institut Curie, Sorbonne Université (see https://institut-curie.org/team/levy).







References: 1. Jani, R. A., Cicco, A. Di, Keren-Kaplan, T., Vale-Costa, S., Hamaoui, D., Hurbain, I., Tsai, F.-C., Dimarco, M., Macé, A.-S., Zhu, Y., Amorim, M. J., Bassereau, P., Bonifacino, J. S., Subtil, A., Marks, M. S., Lévy, D., Raposo, G., and Delevoye, C. (2021) PI4P and BLOC-1 remodel endosomal membranes into tubules. *bioRxiv*. 10.1101/2021.10.21.465321

2. de la Mora, E., Dezi, M., Di Cicco, A., Bigay, J., Gautier, R., Manzi, J., Polidori, J., Castaño-Díez, D., Mesmin, B., Antonny, B., and Lévy, D. (2021) Nanoscale architecture of a VAP-A-OSBP tethering complex at membrane contact sites. *Nat. Commun.* **12**, 1–14

3. Lévy, D., Di Cicco, A., Bertin, A., and Dezi, M. (2021) [Cryo-electron microcopy for a new vision of the cell and its components]. *Med. Sci. (Paris).* **37**, 379–385