Proposition de stage M2

Master Systèmes Biologiques et Concepts Physiques, Sorbonne Université

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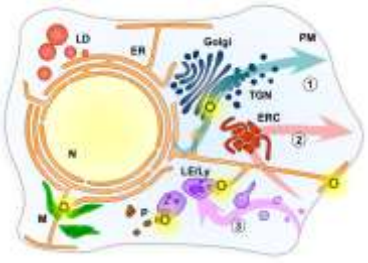
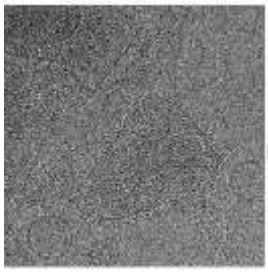
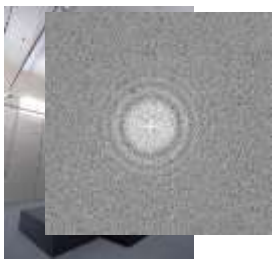
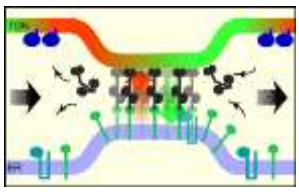
Deciphering communication between cell organelles at subnanometric resolution by cryo-EM

ENCADRENTE de Stage : Manuela Dezi

Cryo-electron microscopy (cryo-EM) is ana imaging method that provides information at atomic resolutions of purified protein and subnanometric resolutions directly in cellulo. This approach, awarded by the Nobel Prize in Chemistry in 2017, combined with advanced computational analyses and deep learning developments is changing our vision of the cell. In this context, our team is interested in the functions associated with membranes and the 3D architecture of membrane proteins. The Master 2 internship is part of our research on how communication occurs within the cell.

Within the cell, organelles communicate with each other thanks to vesicles that traffic between the compartments. In recent years, another mode of communication has been discovered. It consists of proteins that directly connect two facing membranes of different compartments. Thus, the endoplasmic reticulum unifies the entire cell through these contact site membranes MCS. Within these contacts, binding proteins also perform major cell functions such as lipid transport, calcium signaling or organelle inheritance. We have been able to understand how a contact is formed between VAP, a transmembrane protein of ER and OSBP a cholesterol transport protein. In particular, we have shown that disorder is essential for dynamics and function within the confined space of the MCS (Dev. Cell 2019). We have also shown that the flexibility and elasticity of VAP-A modulates the geometry of the MCS and the separation between the facing membranes. We believe that thanks to the flexibility of VAP-A, contact areas can include proteins of different sizes and create a localized multi-protein functional area. To support this hypothesis, the student will create in vitro MSCs from those already designed in the lab with VAP with different flexibility and dimensions. Once formed, the MCS will be analyzed by cryo-EM and cryo-tomography. The goal is to decipher the behavior of VAP in a confined space at subnanometric resolution. These results will be compared with in cellulo experiments carried out by our collaborators (B. Antonny, IPBC, Valbonne, Cell 2013, EMBO J. 2017)

The student must have training in biophysics, an interest in cryo-EM, computational analysis and in vitro approaches. 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 group in Institut Curie, Sorbonne Université (see https://science.institut-curie.org/research/multiscale-physics-biology-chemistry/umr168-physical-chemistry/team-levy.