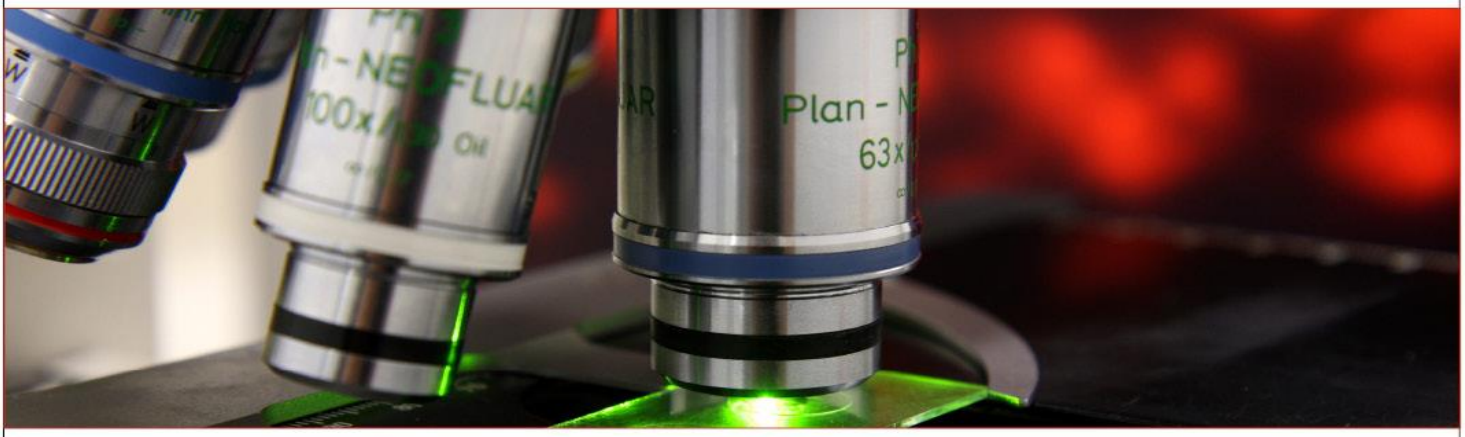
SÉMINAIRES ET CONFÉRENCES



Jomaa Ahmad

Institute of Molecular Biology and Biophysics, ETH Zürich, Switzerland.

« Mechanism of co-translational protein targeting to the endoplasmic reticulum by the mammalian signal recognition particle. »

Almost 30% of the cell proteome consists of membrane and secretory proteins that are delivered co-translationally to the endoplasmic reticulum membrane (ER) in eukaryotes and to the plasma membrane in bacteria. The process involves the function of the universally conserved signal recognition particle (SRP) and its receptor (SR), in a multi-step pathway that recruits the translating ribosome to the Sec translocon on the membrane. Perturbation of this pathway has been linked to the onset of disease particularly to severe congenital neutropenia. Mammalian SRP and SR are compositionally and structurally more complex than their bacterial counterparts with a number of eukaryotic-specific features with unknown regulatory roles. How eukaryotic SRP and SR transition from cargo recognition in the cytosol to the late stages of the targeting pathway on the membrane is a long-standing question. Using a cell-free translation system from rabbit reticulocyte lysate, we trapped molecular snapshots in the targeting pathway and then determined their structures by single particle cryo-EM. We also resolved intermediates in this pathway assembled with a mutant SRP54$_{G226E}$, which is identified in patients with severe congenital neutropenia. Combined with biochemical experiments, our structures reveal the molecular mechanism for co-translational protein targeting to the ER by the mammalian SRP. The cryo-EM structures of complexes assembled with SRP mutants uncover intermediates along the targeting pathway that provide structural and functional basis for this disease in humans.

Le lundi 10 mai 2021, 11h30

Invité de Pascale Legault

Faculté de médecine
Département de biochimie et médecine moléculaire
Université de Montréal