Soutenance

THESE

Mercredi 19 Février 2020 à 14h30

Salle des séminaires IBS

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Cryo-EM characterisation of an enterobacterial stress response system

Thèse de Doctorat de l'Université de Grenoble

The field of electron microscopy has undergone rapid transformation in the past few years. It has become one of the most powerful techniques for investigating macromolecular complexes, providing unprecedented structural insights into the fundamental processes of cellular life. In this thesis, I use cryo electron microscopy and negative stain electron microscopy to investigate two biological systems. The first is an enterobacterial protein triad formed of the *E. coli* proteins LdcI, involved in the acid stress response, and RavA and ViaA, which sensitise *E. coli* to aminoglycosides. I show that the AAA+ ATPase RavA exists in two distinct conformational states, shedding insight into its ATPase mechanism and revealing unexpected mechanistic similarities to the well-characterised unfoldase ClpX. I also explore the effects of fluorescent protein tags on the structure and function of LdcI, in order to facilitate super-resolution fluorescence microscopy. The second complex is the mitochondrial Complex I assembly complex, which is composed of ACAD9, ECSIT and NDUFAF1 and is involved in the maturation of respiratory Complex I in mitochondria. I investigate the ACAD9-ECSITCTD subcomplex using cryo-EM, providing insights into the structure of ACAD9, the location of the ECSITCTD binding site and the release of the FAD cofactor of ACAD9 upon ECSITCTD binding. Finally, in conjunction with biochemical and biophysical analysis, I place the structural information presented in this thesis in a biological context and lay a platform for future studies of both protein complexes.