Grenoble Alliance for Integrated Structural & Cell Biology

GRAL MASTER 2 RESEARCH SCHOLARSHIP - Program 2017 - 2018

INTERNSHIP PROPOSAL

Institute and Group: IBS, group DYNAMOP

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Research project title: Characterization of the organization of enzymes involved in heparan sulfate proteoglycan synthesis by super-resolution microscopy

5 Keywords to describe the project: Golgi apparatus; Glycosylation; Fluorescence Microscopy; PALM microscopy; Fluorescent proteins

Description of the project (aims, experimental techniques, recommended background):
The Golgi apparatus serves as a hub for sorting proteins in the secretory pathway but also as a platform for glycosylation. The proper pattern of glycosylation relies on the organization of the modifying enzymes within the cisternae of the Golgi apparatus and an altered enzyme expression and organization can be found in cancer. The project aims at characterizing the organization of the enzymes involved in a particular type of glycosylation, the formation of the heparan sulfate proteoglycans, the major topic of investigation of the team of Hugues Lortat-Jacob at the IBS. This characterization will be performed by PhotoActivated Localization Microscopy (PALM) using an instrument developed in the team of Dominique Bourgeois at the IBS. It will make use of phototransformable fluorescent proteins developed in the team, suitable for PALM and for the oxidizing environment of the Golgi apparatus. The project will be done in the team of Dominique Bourgeois and will focus on enzymes that are under biophysical and structural investigation in the team of Hugues Lortat-Jacob. It will involve molecular cloning, mammalian cell culture and PALM as well as other fluorescence microscopy approaches like timelapse and FRET. The recruited student will have a background in biology or physics and will show an interest for eukaryotic cell biology and fluorescence microscopy.

Relevant publications of the team:

1. Adam, V., Berardozzi, R., Byrdin, M., and Bourgeois, D. (2014). Phototransformable fluorescent proteins: Future challenges. Curr. Opin. Chem. Biol. 20, 92–102.

2. El Khatib, M., Martins, A., Bourgeois, D., Colletier, J.-P., and Adam, V. (2016). Rational design of ultrastable and reversibly photoswitchable fluorescent proteins for super-resolution imaging of the bacterial periplasm. Sci. Rep. 6, 18459–18459.

3. Préchoux, A., Halimi, C., Simorre, J.-P., Lortat-Jacob, H., and Laguri, C. (2015). C5-epimerase and 2-O-sulfotransferase associate in vitro to generate contiguous epimerized and 2-O-sulfated heparan sulfate domains. ACS Chem. Biol. 10, 1064–1071.