Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

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BioSanté, Biomics team
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Title of the M2 research internship:
Real-time characterization of the ubiquitin-proteasome-dependent proteolytic system by fluorescence microscopy: confirmation of the existence of a 4-hour rhythm of protein degradation in mammalian cells

Project summary:
The synthesis of proteins and their degradation play a major role in the way our cells function, in particular by helping to maintain the abundance of proteins. The abundance of proteins in the cell is regulated in a complex way at the transcriptional, translational and post-translational levels. One of the dominant regulatory pathways of protein degradation occurs via the Ubiquitin-Proteasome system (UPS). We propose to identify, at a molecular level, a newly discovered 4h ultradian rhythm of protein degradation seen hitherto only at level of single cells in total dry mass. This promises to reveal how the UPS regulates degradation during the cell cycle. To do this we will use fluorescence in a variety of human cells to visualize proteasome activity in real time, thus extending the previous lensless imaging techniques. We will test the hypothesis that the proteasome is a four hour pacemaker, which can produce pulsatile dynamics in the cell mass. The project should add a new perspective to quantitative proteolysis studies. We aim to determine the function of this massive protein recycling in order to answer the following questions: does it enable adaptation to acute microenvironmental changes at a low cost in energy, is it a way to “reboot” periodically post-translational modifications of proteins or is it part of a defence system against pathogens?

Keywords:
proteolysis, Biological Rhythm, Ubiquitin proteasome system

Relevant publications of the team:
L. Ghenim, C. Allier, P. Obeid, JY Fortin, M. Balakirev, X. Gidrol, Scientific Reports (2021) 11:1290