Master Biologie Moléculaire et Cellulaire 'BMC',
Université Paris Cité - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage de M2, 2024-2025

Unité INSERM ou CNRS ou Université : **Institut Jacques Monod** **(UMR 7592 CNRS/Univ. Paris-Cité)** **Intitulé Equipe :** **Membrane trafficking, ubiquitin and signaling.** **ED d'appartenance : BioSPC** **Responsable de l'Equipe : S. Léon**	**Responsable du Stage : Sébastien LEON** **Contacts** Adresse **: Institut Jacques Monod** **15, rue Helene Brion** **75013 Paris** Email : **sebastien.leon@ijm.fr** Tel : **01 57 27 80 57**

Titre du projet : Discovery of new cellular functions of protein phosphatase PP1

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

The function or fate of many proteins is regulated by post-translational modification events such as **phosphorylation** or **ubiquitylation**. This regulation is at the heart of most if not all cellular functions and biological processes, and can cause pathologies when deregulated. For many years, our lab studied how nutrients are sensed to activate nutrient-signaling pathways which in turn allow the onset of an adaptive response. In particular, using **yeast** as a model organism, we focused on nutrient-regulated membrane protein **trafficking**. We identified a regulatory phosphatase of the **PP1** family in charge of controlling nutrient-regulated endocytosis of nutrient transporters. This occurs through a nutrient-sensitive dephosphorylation of an arrestin involved in endocytosis. By quantitative proteomics, we recently identified new **interactants** of PP1 involved in membrane trafficking and ubiquitin homeostasis. We also discovered that PP1 is associated to the **lysosomal membrane**, suggesting new functions that may be compartment-specific. The aim of this project is to (i) confirm that the protein partners identified are bona fide interactants, (2) understand the molecular basis of the association of PP1 to the lysosomal membrane and (3) study the functional relevance of these interactions and this localization. Various methods will be used, ranging from molecular biology and genetics to generate tools (mutants, truncated proteins, GFP-tagged proteins), to biochemical techniques (western-blots, co-IPs) to study protein-protein interactions and analyze protein phosphorylation, and microscopy analysis to reveal potential defects in endocytosis

Publications de l'équipe relatives au projet de stage (max 5) (étudiants en thèse soulignés)

-Laussel C, Albanese V, Garcia-Rodriguez FJ, Ballin A, Defenouillere Q, Leon S. 2-deoxyglucose transiently inhibits yeast AMPK signaling and triggers glucose transporter endocytosis, potentiating the drug toxicity. **PLoS Genet**. **2022**;18(8):e1010169. http://doi.org/10.1371/journal.pgen.1010169

-Defenouillère Q, Verraes A, Laussel C, Friedrich A, Schacherer J, Leon S. The induction of HAD-like phosphatases by multiple signaling pathways confers resistance to the metabolic inhibitor 2-deoxyglucose. **Science Signaling. 2019**;12(597):aaw8000. http://doi.org/10.1126/scisignal.aaw8000

-Hovsepian J, Defenouillere Q, Albanese V, Vachova L, Garcia C, Palkova Z, Leon S. Multilevel regulation of an alpha-arrestin by glucose depletion controls hexose transporter endocytosis. **J Cell Biol. 2017**;216(6):1811-31. http://doi.org/10.1083/jcb.201610094

-Becuwe M, Leon S. Integrated control of transporter endocytosis and recycling by the arrestin-related protein Rod1 and the ubiquitin ligase Rsp5. **eLife. 2014**;3:03307. http://doi.org/10.7554/eLife.03307

-Becuwe M, Vieira N, Lara D, Gomes-Rezende J, Soares-Cunha C, Casal M, Haguenauer-Tsapis R, Vincent O, Paiva S, Léon S. A molecular switch on an arrestin-like protein relays glucose signaling to transporter endocytosis. **J Cell Biol. 2012**;196(2):247-59. http://doi.org/10.1083/jcb.201109113