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

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

Unité INSERM ou CNRS ou Université : CNRS UMR8226 **Intitulé Equipe : Dynamique Membranaire et Modifications Post-Traductionnelles http://lbmce.ibpc.fr/fr/notre-laboratoire/** **ED d'appartenance : Complexité du Vivant (ED515)** **Responsable de l'Equipe : Mickael Cohen**	**Responsable du Stage : Mickael Cohen** **Contacts** Adresse : **Institut de Biologie Physico-Chimique - 13, rue Pierre et Marie Curie 75005 Paris** Email : cohen@ibpc.fr Tel : **01 58 41 51 89**

Titre du projet : Mechanism and Regulation of Mitochondrial Dynamics

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

Mitochondria constitute a remarkably dynamic cellular network in contact with most organelles. The morphology of this network is shaped by frequent events of fission and fusion of mitochondrial membranes, which are essential to shape the ultra-structure of the mitochondrial compartment and are thus also crucial for all mitochondrial functions. It is therefore not surprising that defects in mitochondrial fusion and fission are associated with numerous pathologies and severe neurodegenerative syndromes as well as important developmental disorders, especially.

Mitochondrial Fusion and fission are both mediated by Dynamin-Related Proteins (DRPs). DRPs are large GTPases that bind biological membranes and shape the form of lipid bilayers. To promote mitochondrial fission, DRPs (DRP1 in metazoans, Dnm1 in yeast) are recruited at mitochondrial contact sites with the Endoplasmic Reticulum where they assemble into spirals around mitochondrial tubules. GTP hydrolysis within these spirals induces their constriction followed by separation of mitochondria. The mitofusins (MFN1 and MFN2 in mammals; Fzo1 in yeast) and OPA1 (Mgm1 in yeast) are two other sets of DRPs that mediate fusion of mitochondrial outer and inner membranes, respectively.

Our team focuses on the mechanism by which mitofusins promote membrane anchoring and lipid bilayers merging in vitro; the mechanism by which the Ubiquitin-Proteasome System (UPS) regulates mitofusin-mediated fusion in vivo; an interesting crosstalk between the UPS and Mitophagy (the degradation of mitochondria by autophagy); an unprecedented analysis of mitochondrial morphology by Super-Resolution fluorescence microscopy.

The M2 project will focus on one of these topics based on the candidate background among multidisciplinary approaches, including genetics, biochemistry, cell biology, cellular imaging or physico-chemical and structural biology. Besides elucidating molecular mechanisms underlying mitochondrial fusion and fission or mitophagy, the project will generate new concepts on general membrane trafficking events and will allow better apprehending the molecular basis of numerous neuropathies directly caused by defects in mitochondrial dynamics.

Publications de l'équipe relatives au projet de stage (max 5)

Alsayyah C., Singh M.K., Morcillo-Parra M.A. , Cavellini L., Shai N., Schmitt C., Schuldiner M., Zalckvar E., Mallet, A. Belgareh-Touzé N., Zimmer C. and COHEN M.M.* (2024) Mitofusin-mediated contacts between mitochondria and peroxisomes regulate mitochondrial fusion. Plos Biology 22 (4), e3002602

Singh M.K., Cavellini L., Kunz C., Lelek M., Bomme P., Belgareh-Touzé N., Mallet, A., Dietrich L., Zimmer C. and COHEN M.M.* (2024) A constricted mitochondrial morphology optimizes respiration. bioRxiv, 2024.03. 21.582105

Belgareh-Touzé N.*, Cavellini L. and COHEN MM.* (2017) Ubiquitylation of ERMES components by the E3 ligase Rsp5 is involved in mitophagy. Autophagy. 13:114-132. (50 citations)

Cavellini L., Meurisse J., Findinier J., Erpapazoglou Z., Belgareh-Touzé N., Weissman AM. and COHEN MM.* (2017) An ubiquitin dependent balance between mitofusin turnover and fatty acids desaturation regulates mitochondrial fusion. Nature Communications. 8: 15832 (24 citations)

Brandt T., Cavellini L., Kühlbrandt W.* and COHEN M.M.* (2016) A mitofusin-dependent docking ring complex triggers mitochondrial fusion in vitro. eLife. (5) doi: 10.7554/eLife.14618. (112 citations) (F1000 Highlight). ***1 page maximum SVP !***