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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
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Fiche de Projet de Stage M2, Année 2022-2023

Unité INSERM ou CNRS ou Université : CNRS UMR8226 **Intitulé Equipe : Dynamique Membranaire et Modifications Post-Traductionnelles** **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 Fusion

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

Mitochondria are organelles that are not isolated from each other but that constitute a real and remarkably dynamic cellular network. The morphology of this network is shaped by movement of mitochondria along cytoskeletal tracks associated with extraordinary frequent events of fission and fusion of mitochondrial membranes. These fusion and fission processes are essential to shape the ultra-structure of the mitochondrial compartment and are thus also crucial for all mitochondrial functions including oxidative phosphorylation, calcium signalling, apoptosis or lipid metabolism. 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.

From a molecular standpoint, fusion and fission of mitochondrial membranes are both mediated by large GTPases that belong to the super-family of Dynamin-Related Proteins (DRPs). While ability of DRPs to mediate membrane fission is well documented, the mechanism employed by these proteins to promote membrane fusion requires additional fundamental insights which represents a tremendous matter of interest.

The goal of the project thus consists in dissecting the mechanism and the regulation of mitochondrial fusion with a specific focus on the yeast mitofusin Fzo1 which mediates the tethering and fusion of mitochondrial outer membranes. To this end, multidisciplinary approaches will be used including genetics, biochemistry, cell biology, cellular imaging as well as physico-chemical and structural biology.

Besides elucidating molecular mechanisms underlying mitochondrial fusion, the present project is expected to generate new concepts that may not only apply to general membrane trafficking events but should also participate in 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)

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. (79 citations) (F1000 Highlight)

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 (19 citations)

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. (38 citations)

De Vecchis D., Cavellini L., Baaden M., Henin J., COHEN MM.* and Taly A.* (2017) A membrane-inserted structural model of the yeast mitofusin Fzo1. Scientific Reports. 7: 10217 (22 citations)

Brandner A., De Vecchis D., Baaden M., COHEN MM.* and Taly A.* (2019) Physics-based oligomeric models of the yeast mitofusin Fzo1 at the molecular scale in the context of membrane docking. Mitochondrion. 49, 234-244 (8 citations)

COHEN MM.* and Tareste D.* (2018) Recent insights into the structure and function of Mitofusins in mitochondrial fusion. F1000Research. 7 (20 citations)

1 page maximum SVP !