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 2021-2022

Unité INSERM ou CNRS ou Université : UMR8226 **Intitulé Equipe : Dynamique Membranaire et Modifications Post-Traductionnelles** **ED d'appartenance : CDV ED515** **Responsable de l'Equipe : Mickael Cohen**	**Responsable du Stage : Mohammad Ozeir** **Contacts** Adresse : IBPC, UMR8226, 13 rue Pierre et Marie Curie 75005 Paris Email : ozeir@ibpc.fr ou cohen@ibpc.fr Tel : 01 58 41 51 89

Titre du projet : Structural and mechanistic investigation on mitochondrial fusion.

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

Mitochondria are dynamic organelles implicated in a range of cellular functions. These double membraned organelles assemble as a network which continually changes its morphology, shape, and size. This is orchestrated by opposing events of fusion (membrane interconnection) and fission (membrane fragmentation), referred as mitochondrial dynamics. Dysfunctional mitochondrial dynamics is linked with a range of diseases that especially affect the nervous system.

Pivotal components mediating the fusion and fission process of the outer/inner membrane(s) belong to the dynamin family of GTPases. While the ability of DRPs to mediate membrane fission is well documented, the mechanism of outer-membrane Fusion DRPs, named mitofusins remains poorly understood. Yet, mitofusins were originally identified in Drosophila through their implication in spermatogenesis. Moreover, mutations in the human mitofusin MFN2 cause the Charcot–Marie–Tooth disease and are linked to the etiology of Parkinson disease. Consequently, structural and biophysical data on mitofusins are of paramount importance.

For this purpose, this M2 project we will focus on Fzo1, the yeast mitofusin, as a model to understand the mitochondrial-outer- membrane fusion mechanism. Adopting a multidisciplinary approach, we will aim at purifying Fzo1 and resolve its structure employing either crystallography or Cryo-Electron-Microscopy. Purified Fzo1 will then be used to launch physico-chemical studies and liposome assays. In fine, we will aim at elucidating the molecular mechanism underling mitochondrial fusion. This will ultimately provide a better understanding of the molecular basis behind neuropathies caused by defects in mitochondrial dynamics

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

- 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 (7 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 (19 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 (17 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. (30 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. (67 citations) (F1000 Highlight)