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 : **INSERM U1266** **Intitulé Equipe : Dynamique endosomale dans les neuropathies** **ED d'appartenance : BioSPC, ED 562** **Responsable de l'Equipe : G van Niel**	**Responsable du Stage : G van Niel** **Contacts** Adresse : Institut de Psychiatrie et Neurosciences de Paris (IPNP). 102 rue de la Santé, 75014 , Paris Email :guillaume.van-niel@inserm.fr Tel : 33 1 40 78 92 36

Titre du projet : Role of membrane contact site during lysosome reformation.

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

The endosomal pathway is composed of continuum of compartments that sort endocytosed proteins and lipids toward recycling, lysosomal degradation and exosomal secretion[1]. To do so, the **endosomes** undergo multiple morphological changes through their maturation that allows the generation of export tubules or intraluminal vesicles. A new level of regulation of endosomal maturation involves non-fusogenic apposition of the membranes of distinct organelles such as those of endosomes and endoplasmic reticulum, which are called **membrane contact sites** (MCS). MCS are required for lipid exchange between compartments and have been recently implicated in the **generation of export tubules**. Our laboratory has demonstrated the role of the complex PIKfyve, which generate Pi3,5P2, in the generation of endosomal tubules[2] from endolysosomes and the relevance of this process in the recycling of lysosomal materials and physiological amyloid formation [3-5]. We have identified new interactants of the PIKfyve complex that are involved in MCS required for endosomal tubulation and could act during lysosomal reformation. Importantly, our unpublished data suggest that such process may have proeminent role in the metabolism of the amyloid Abeta peptide that is central in the etiology of the **Alzheimer's Disease**.
Our project aims at better understanding the role of MCS in lysosomal reformation and its relevance in pathological amyloid metabolism. We will first investigate the role of the newly identified interactants during PIKfyve regulated lysosomal reformation with a specific focus on generation and function of MCS during this process. Then we will assess the relevance of such process in the etiology of Alzheimer's Disease and in particular in the homeostasis of pathological amyloids. For this project, the applicant will will profit from an international environment and use and apply a combine **imaging** (live cell, electron microscopy, correlative microscopy), **biochemistry** and molecular biology approaches on neuronal/glial cell lines and primary cells.

Publications de l'équipe, relatives au stage proposé

1. Bécot A, Volgers C, van Niel G. Transmissible Endosomal Intoxication: A Balance between Exosomes and Lysosomes at the Basis of Intercellular Amyloid Propagation. Biomedicines. 2020.
2. van Niel G, et al. Shedding light on the cell biology of extracellular vesicles. Nat Rev Mol Cell Biol. 2018
3. Bissig C et al. PIKfyve activity regulates reformation of terminal storage lysosomes from endolysosomes. Traffic. 2017 Nov
4. Bissig et al, PIKfyve complex regulates early melanosome homeostasis required for physiological amyloid formation. J Cell Sci. 2019 Feb
5. van Niel G. Study of Exosomes Shed New Light on Physiology of Amyloidogenesis. Cell Mol Neurobiol. 2016