Sciences de la Vie et de la Santé
Master BCPP, Universités Paris Descartes – Paris Diderot

Spécialité : **Biologie et Développement Cellulaires**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : INSERM U1163 –Institut Imagine **Intitulé Equipe :** Laboratoires des Maladies rénales héréditaires **ED d'appartenance :** BioSPC **Responsable de l'Equipe :** Sophie Saunier	**Responsable du Stage :** Alexandre Benmerah **Contacts** Adresse : 24 Bd Montparnasse, 75015 Paris Email : alexandre.benmerah@inserm.fr Tel :

Titre du projet: Characterization of the ciliary functions of a GPCR family, the target of a potential new therapeutic approach for renal ciliopathies.

Résumé du Projet de Stage

Ciliopathies are highly heterogeneous **genetic diseases** caused by mutations in genes encoding proteins playing key functions at the **primary cilium** (1), a ubiquitous organelle controlling numerous signaling pathways during development and tissues homeostasis. **Nephronophthisis** (NPH) is one of the most frequent manifestations in ciliopathies (1) and represents the morbidity factor for the patients for which the kidney graft is the only therapeutic issue. The lab was involved in the identification of more than half of the 22 NPHP genes (1) and developed strategies to identify molecules able to rescue ciliopathy phenotypes in model cell lines. This screen allowed the identification of an interesting **molecule** targeting a family of **G protein-coupled receptor** (GPCR) previously identified as involved in functions at cilia. The goal of this project is to characterize the expression and ciliary localization of these receptors in kidney cells, their function at cilia as well as the impact of NPHP genes on these processes using model kidney epithelial cells collected from patients and cell lines. We also aim to use in vivo models for NPH (zebrafish or mouse) to validate these in vitro observations and to validate the use of this drug as a potential new therapeutic approach for renal ciliopathies.

1-Stokman M, Saunier S, Benmerah A https://doi.org/10.3389/fcell.2021.653138

Publications de l'équipe, relatives au stage proposé

- Reilly ML, Stokman MF, Magry V, … Saunier S, Giles RH, **Benmerah A**. Loss-of-function mutations in KIF14 cause severe microcephaly and kidney development defects in humans and zebrafish. Hum Mol Genet. 2019 Mar 1;28(5):778-795.
- Macia MS…, Saunier S*, Hildebrandt F*, **Benmerah A***. Mutations in MAPKBP1 Cause Juvenile or Late-Onset Cilia-Independent Nephronophthisis. Am J Hum Genet. 2017 Feb 2;100(2):323-333. * equal contributions
- Bizet AA, Becker-Heck A, …, **Benmerah A***, Saint-Mezard*, P, Saunier S*. Mutations in TRAF3IP1/IFT54 reveal a new role for IFT proteins in microtubule stabilization. Nat Commun. 2015 Oct 21;6:8666. * equal contributions
- Failler M, Gee HY, Krug P, Kim J, **Benmerah A**, Hildebrandt F, Saunier S. Mutations of CEP83 cause infantile nephronophthisis and intellectual disability. Am J Hum Genet. 2014 Jun 5;94(6):905-14.
- Ghossoub R, Hu Q, Failler M, … Jamesnelson W, **Benmerah A**. Septins 2, 7 and 9 and MAP4 colocalize along the axoneme in the primary cilium and control ciliary length. J Cell Sci. 2013 Jun 15;126(Pt 12):2583-94.