Sciences de la Vie et de la Santé
Master BMC, Universités Paris Cité

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2023-2024

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

Titre du projet: Impact of patient variants in the function and localization of *NPHP3* at the primary cilium.

Ciliopathies are highly heterogeneous **genetic diseases** caused by mutations in genes encoding proteins playing key functions at the **primary cilium**, a ubiquitous organelle controlling numerous signaling pathways during development and tissues homeostasis. **Nephronophthisis** (NPH) is one of the most frequent kidney manifestation in ciliopathies 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 (see ref 1 below for review). We recently developed different in vitro and in vivo models for the *NPHP3* gene responsible for isolated NPH and severe syndromic fetal syndromic forms. NPHP3 is a key component of the Inversin compartment, a fibrilloid polymer made of 4 proteins present at the proximal end of cilia which play a key role in ciliary signaling. The exact function of the Inversin compartment and of NPHP3 within this compartment are currently not understood.
The proposed M2 project is part of the Cilia-AI European consortium project and aim at using results AI-based tool analyses to better understand the organization of the Inversin compartment, to investigate the impact of patient variants on this complex and to identify new ciliary partners of NPHP3 through in silico screening. Complementary to these in silico approach, NPHP3 KO kidney tubular cells will be transfected with GFP-tagged NPHP3 patient variants. The consequences of patient variants on the ciliary localization of NPHP3 will be analyzed by super resolution fluorescence microscopy. These cells will also be used to validate the potential new partners identified by in silico approaches and to investigate their localization within ciliary subdomains.

Publications de l'équipe, relatives au stage proposé
Former Postdocs and PhD students are underlined

1- Stokman M, Saunier S and **Benmerah A**. Renal Ciliopathies: Sorting Out Therapeutic Approaches for Nephronophthisis. Front. Cell Dev. Biol., 13 May 2021 | https://doi.org/10.3389/fcell.2021.653138

- Tata A, Rocha G, Hureaux M, Serafin AS, Porée E, Menguy L, Goudin N, Cagnard N, Gréau L, Fila M, Briseño-Roa L, Annereau JP, Saunier S, **Benmerah A**. Prostaglandin Analogs and Eupatilin as Treatments for Nephronophthisis. Kidney Int Rep. 2025 May 2;10(8):2821-2835. https://doi.org/10.1016/j.ekir.2025.04.060

- Hugo Garcia*, Alice Serafin*, …, **Alexandre Benmerah°**, Marion Delous°, Luis Briseño-Roa°, Sophie Saunier°. Agonists of prostaglandin E2 receptors as potential first in class treatment for Nephronophthisis and related ciliopathies. PNAS 2022 May 3; 119(18): e2115960119. https://doi.org/10.1073/pnas.2115960119 *contributed equally °contributed equally

- Reilly ML°, Ain NU°, Muurinen M, Tata A, Huber C, … Cormier-Daire V*, **Benmerah A***, Makitie O*. Biallelic KIF24 Variants Are Responsible for a Spectrum of Skeletal Disorders Ranging From Lethal Skeletal Ciliopathy to Severe Acromesomelic Dysplasia. J Bone Miner Res. 2022 Sep;37(9):1642-1652. doi: 10.1002/jbmr.4639. *,°contributed equally