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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
https://master2bdc.ijm.fr/
Fiche de Projet de Stage de M2, 2026-2027

Unité INSERM ou CNRS ou Université : Inserm U1163 – Institut Imagine **Intitulé Equipe :** Laboratory of Inherited Kidney Diseases **ED d'appartenance :** BioSPC **Responsable de l'Equipe :** Sophie SAUNIER	**Responsable du Stage :** Amandine VIAU **Contacts** Adresse : 24 Boulevard du Montparnasse 75015 Paris Email : amandine.viau@inserm.fr Tel : +33 1 42 75 43 41

Titre du projet : Interplay between LKB1 and primary cilia in proximal tubule homeostasis

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

The **kidney tubule** plays a central role in **acute kidney injury** (AKI) and **chronic kidney disease** (CKD). In both conditions, tubular cells switch their **metabolism** from fatty acid oxidation to glycolysis and secrete cytokines that promote **fibro-inflammation** with immune cells recruitment and myofibroblasts activation. Targeting metabolic rewiring, fibro-inflammation and/or cell death are potential therapeutic options for CKD and AKI. Yet, a better understanding of the master regulators governing these events is critical to allow more efficient interventions.

The protein liver kinase B1 (**LKB1**) is a **master regulator of cell metabolism** and localizes to the **primary cilium**, a solitary microtubule-based expansion of the plasma membrane. **In the kidney**, the primary cilium projects into the lumen of the tubules and acts as a **cell antenna** to integrate mechanical and chemical cues delivered by urine flow. We showed that, tubular *Lkb1* invalidation resulted in inflammation and a drop in the expression of proximal tubule transporters leading to normoglycemic glycosuria and an increased phosphaturia. Unexpectedly, kidney inflammation and proximal tubules defects were also present in cilia-depleted *Lkb1* knock-out animals. However, cilia ablation in LKB1 deficiency resulted in a **desquamation of proximal tubular cells**, kidney failure and premature death, a phenotype strikingly reminiscent of severe AKI. These surprising results indicate that **LKB1 exerts key roles in the proximal tubule** and further pinpoint an **unanticipated function of primary cilia**, which appear essential for proximal cells maintenance in LKB1 deficiency.

The aim of this project is to investigate the interaction between LKB1 and ciliary signalling in proximal tubules. We will profile the transcriptome of proximal micro-dissected tubules and analyze the metabolic changes brought by LKB1 and/or cilia ablation by performing metabolomics on whole kidneys. To complement these unbiased screens, we will use transmission electron microscopy to perform comprehensive ultrastructural analysis of tubular cells and mitochondria. In parallel we will explore proximal tubule cell death (apoptosis, necroptosis, lipid peroxidation) by immunofluorescence, western blot and qPCR.

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

Martin J*, Serafin AS*, et al. *Developmental switch dichotomizes kidney response to Nphp3 inactivation and treatment outcome*. **bioRxiv**. **2026**. doi.org/10.64898/2026.05.21.726570

Aka A*, Martin J*, et al. *A cilia-dependent inflammatory programme links bacterial detection to kidney disease*. **bioRxiv**. **2026**. doi.org/10.64898/2026.04.24.720658

Ferri G, et al. *IL1b is induced in nephronophthisis but does not mediate kidney damage*. **Genes & Diseases**. **2025**. doi.org/10.1016/j.gendis.2025.101687

Quatredeniers M, et al. *The renal inflammatory network of nephronophthisis.* **Hum. Mol. Genet. 2022**. doi.org/10.1093/hmg/ddac014

Viau A*, Bienaimé F*, et al. *Cilia-localized LKB1 regulates chemokine signaling, macrophage recruitment, and tissue homeostasis in the kidney*. **EMBO J**. **2018**. doi.org/10.15252/embj.201798615