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, 2024-2025

Unité INSERM ou CNRS ou Université : Institut Necker Enfants Malades (INEM) INSERM U1151-CNRS UMR 8253 **Intitulé Equipe :** Maladie Rénale Chronique, Mécanisme et Thérapeutique **ED d'appartenance :** BIOSPC **Responsable de l'Equipe :** Fabiola Terzi	**Responsable du Stage :** Nicolas Dupont **Contacts** Adresse : INEM, 156 Rue de Vaugirard 75015 Paris Email : nicolas.dupont@inserm.fr Tel : 33(0)140615388

Titre du projet : Interplay between autophagy, inflammation and fibrosis in kidney epithelial cells.

Résumé du Projet de Stage (mots clés en gras)

This project will aim to study the molecular and cellular events downstream the impairment of **autophagy** that can contribute to drive the progression of **chronic kidney disease** (CKD). CKD, one of the major public health challenges, is characterized by a progressive decline in renal function which can occur regardless of the initial cause of renal damage. Autophagy is a lysosomal degradation pathway that plays crucial roles in cellular homeostasis, notably during **mechanical stress response**. This project is a direct follow-up to our work showing an impairment of autophagy in kidney epithelial cells (KECs) submitted to pathological fluid flow condition (shear stress of 3 dyn/cm^2 (versus physiological flow condition (shear stress of 1 dyn/cm^2). We hypothesize that those impairments in KECs submitted to pathological flow condition lead to the (i) cellular dedifferentiation and impairment of the tubular function (ii) the production and the secretion of **pro-inflammatory** and **profibrotic** factors which contribute to the amplification of kidney damage. To challenge this hypothesis, we will use a **microfluidic system** mimicking the pathological unilateral urinary fluid flow applied on renal tubular cells. To carry out this project, biochemical, cellular and molecular biology approaches will be implemented in the laboratory as well as human tissue samples in collaboration with the Necker Hospital.

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

2023. A.Claude-Taupin*, F.Roccio, M.Garfa-Traoré, A.Regnier, M.Burtin, E.Morel, F.Terzi, P.Codogno* and N.Dupont*. YAP-dependent autophagy is controlled by AMPK, SIRT1 and flow intensity in kidney epithelial cells. Nature Communications

2021. Link between autophagy and tissue mechanics. A. Claude-Taupin, P.Codogno* and N.Dupont*. Journal of Cell Science, Sep 1;134(17)

2020 The primary cilium and lipophagy translate mechanical forces to direct metabolic adaptation of kidney epithelial cells, C.Miceli[1], F.Roccio[1], L.Penalva-Mousset, M.Burtin, C.Leroy, I.Nemazanyy, N.Kuperwasser, M.Pontoglio, G.Friedlander, E.Morel, F.Terzi, P.Codogno*, N.Dupont*. Nature Cell Biology.

2019 Interplay between Primary Cilia, Ubiquitin-Proteasome System and Autophagy. Boukhalfa A, Miceli C, Ávalos Y, Morel E*, Dupont N*. Biochimie, Nov, 166:286-292

2016. I Orhon*, N. Dupont*, M. Zaidan, V. Boitez, M. Burtin, A. Schmitt, T. Capiod, A. Viau, I. Beau, E. W. Kuehn, G. Friedlander, F. Terzi, P. Codogno. Primary cilium-induced autophagy controls epithelial cell volume in response to fluid flow. Nature Cell Biology, Jun;18(6):657-67,