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, 2025-2026

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Titre du projet : To decipher the impact of autosomal dominant Parn deficiency in a bleomycin-induced model of pulmonary fibrosis in mice.

Résumé du Projet de Stage

Idiopathic pulmonary fibrosis (IPF) is the most common and severe form of idiopathic interstitial lung disease. Approximately 10% of IPF cases are associated with familial cases. Currently, except from lung transplantation, there are no curative treatments available for IPF patients. In nearly 30% of familial cases, a pathogenic heterozygous variant is detected in a gene that controls telomere homeostasis. Among these, heterozygous variants in "poly(A)-specific ribonuclease" (*PARN*) gene are among the most frequently encountered. However, the biological mechanisms linking these **PARN** variants and pulmonary fibrogenesis remain unknown. Our team aims to understand these biological mechanisms and eventually correct them through targeted therapy in Humans.

Autosomal dominant *Parn* deficient (Parn$^{+/-}$) mice have been obtained and are currently being breeding. Lung fibrosis will be studied in well-established **models of lung fibrosis induced by tracheal administration of bleomycin**. Bleomycin will be administered intratracheally to male *Parn*$^{+/-}$ and *Parn*$^{+/+}$ mice aged 7 to 11 weeks. At 14-days post-bleomycin treatment, the mice will be sacrificed. Together with a PhD student, the master student will analyze these mice. He will **characterize the impact of *Parn* deficiency in this model on inflammation and pulmonary fibrosis** (COL1 expression assessed by qPCR and western-blot, quantification of lung hydroxyproline content and histological morphometry). He will also **assess telomere biology alteration** in these mice. Telomer length will be assessed through Luminex. The impact of *Parn* deficiency on DNA damage pathway activation will be assessed by studying the formation of p53-binding protein 1 (53BP1) and γ-H2AX foci using immunofluorescence. In order to study cell senescence, p16 expression will be evaluated by immunofluorescent microscopy.

The findings from this project will contribute to a broader translational research program focused on ***PARN*-associated pulmonary fibrosis**.

Nb.: no specific training in animal experimentation is required to apply for this project.

Publications de l'équipe relatives au projet de stage

Philippot Q, *et al.* Respirology. 2022 Mar;27(3):226–35
Borie R, *et al.* Eur Respir J. 2022 Dec 22;2201383.
Revy P, *et al.* Nat Rev Genet. 2023 Feb;24(2):86–108.
Ghanem M, *et al.* Am J Respir Crit Care Med. 2024 Dec 5.