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

Unité INSERM U1149 **Intitulé Équipe : CRI** **ED d'appartenance : Bio-SpC** **Responsable de l'Equipe : A. Mailleux / B. Crestani**	**Responsable du Stage : Q. Philippot** **Contacts** Adresse : 16 rue Henri Huchard 75018 Paris, France, Email : quentin.philippot@aphp.fr Tel : 01 40 25 69 18

Titre du projet: To determine the impact of autosomal dominant Parn deficiency on bleomycin-induced pulmonary fibrosis in aged 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 is no curative treatment 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 being breaded. Compared with wild-type mice, 5 months-old *Parn*$^{+/-}$ mice, from the 2nd generation, show reduced pulmonary expression of *Parn*, normal lung development, and similar susceptibility to bleomycin-induced fibrosis, a well-established model of lung fibrosis. Mice have telomeres that are on average 10 times longer than those in humans, which probably explains the absence of increased susceptibility to bleomycin-induced fibrosis in the *Parn*$^{+/-}$ mice studied so far. The susceptibility to bleomycin-induced fibrosis will be studied in aged *Parn*$^{+/-}$ mice (16 months old) from the 4th generation. Together with a PhD student, the master student will analyze these mice. He will **characterize the impact of *Parn* deficiency in this model on 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: 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. To study cell senescence, p21 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**: https://anr.fr/Projet-ANR-25-CE17-5953.

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.