PhD position - Université de Paris - Institut Necker Enfants Malades

PhD Title: Epigenetics of HNF1B-kidney disease: understanding the cellular and molecular mechanisms

Supervisor: Marco Pontoglio

The offer: A fully funded 3 years position in Pontoglio Lab is open for graduate students to study the role played by HNF1B in nephron tubular maintenance.

This PhD programme is funded by the EU through an ITN network "Multidisciplinary training in chronic kidney disease: from genetic modifiers to drug discovery" (TrainCKDis). TrainCKDis gathers top European laboratories, companies, hospitals, and associations involved in the treatment of CKD. Early Stage Researchers will thus benefit from an outstanding interdisciplinary platform integrating nephrology, epidemiology, genetics, cell biology, high-throughput screening, system biology, and metabolomics experts.

The Lab: The group "Epigenetics and Development" led by Marco Pontoglio is located at the "Institut Necker Enfants Malades" (INEM). The INEM is an international biomedical research center located on the Necker Hospital Campus, in the central Montparnasse district in Paris, France. It is supported by the French National Institute of Health and Medical Research (INSERM), the French National Center for Scientific Research (CNRS) and the University of Paris. The close interactions between the research labs and the clinical departments represent a major strength creating a highly dynamic environment. The INEM is the hub for cellular and molecular biology at University of Paris, one of the World's leading universities. The Institute hosts over 300 talented scientists who are working together to promote scientific discoveries in the study of the molecular and cellular mechanisms of human diseases. The research activities of our laboratory focus on the epigenetic mechanisms underlying the establishment of renal cell identity. In particular, the group is involved in the study of the function played by a key transcription factor called HNF1B (Gresh et al EMBO J 2004; Fischer et al Nature Genetics 2006; Verdeguer et al. Nature Medicine 2010; Massa et al Development 2013; Lerner et al NAR 2016).

The project: HNF1B is a transcription factor involved in the epigenetic bookmarking whose mutations are known to be responsible for renal developmental defects and renal disease. The goal of this project is to elucidate the cellular and molecular mechanisms that accounts for the development of renal lesions after HNF1B inactivation in adult kidney. While much is known about the role of HNF1B in kidney development, with mutations in HNF1B being a primary cause of Congenital Abnormalities of the Kidney and Urinary Tract (CAKUT), little is known about its possible function in tissue homeostasis in the adult kidney. With the use of an inducible kidney specific inactivation, our results have shown that when HNF1B is inactivated in adult mouse kidneys there is a rapid and drastic tubular atrophy and interstitial fibrosis. This phenotype recapitulates the traits observed in many HNF1B adult patients. This research project will use transcriptomic analysis (bulk and single cell) and chromatin immunoprecipitation (ChIP-seq) approaches, to assess the identity of the genetic program of HNF1B in adult kidney to clarify the functions played by this transcription factor in adult kidneys. In parallel, the candidate will characterize the cellular events that lead to tubular atrophy and fibrosis.

The candidate: We are interested in rigorous and talented candidates who are passionate about addressing biological questions with potential therapeutic applications. This position is particularly suited for applicants with an enthusiastic interest in molecular and cell biology, epigenetics with a particular emphasis on the analysis and integration of signaling pathways in mouse models. Competences in basic molecular biology technics will be appreciated. The candidate must demonstrate a prompt capacity to adapt to a new environment and to interact with colleagues.

Applications should include a cover letter, a full CV, and the names and addresses of two referees.

Offer Deadline: June 30th, 2020

Beginning of the Fellowship: September 2020

Contact: pontogliolab@gmail.com

Advantages: As EU-funded project, TrainCKDis offer attractive salary to recruited researchers. To find more details, please read the information note of the European Commission.