PhD position - Université de Paris - Institut Necker Enfants Malades

PhD Title: Epigenetics of HNF1B-kidney disease: Identification of modifier genes

Supervisor: Marco Pontoglio

The offer: A fully funded 3 years position in Pontoglio Lab is open for graduate students to study the identification of HNF1B modifier genes in renal disease.

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 epigenetic bookmarking whose mutations are responsible for renal developmental defects and renal disease. One of the most striking observations concerning is the extreme variable phenotype of patients sharing the same familial mutation. HNF1B patients carry heterozygous null mutations that are thought to give rise to haploinsufficiency. These patients present with renal developmental defects whose severity can be extremely variable including kidney agenesis, cystic dysplasia and tubular atrophy. We do not fully understand the molecular mechanism of these dysfunctions and their variable presentation. One of the possible reasons is a differential residual biological activity of HNF1B of each patient. The residual biological activity of HNF1B may depend on the segregation of variants for modifier genes. To identify these genes, we will carry out a CRISPRi genome-wide screening on renal cell lines. The candidate modifier genes identified by the screening will be verified in HNF1B discordant duos, patients carrying the same HNF1B familial mutation but presenting with discordant phenotype.

The candidate: We are interested in rigorous and talented candidates who are passionate about addressing basic biological questions with potential therapeutic applications. This position is particularly suited for applicants with an enthusiastic interest in molecular and cell biology and epigenetics with a particular emphasis on the most recent technological applications (eg CRISPR Library Screening with CRISPRi). 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.