CENTRE DE RECHERCHE
DES CORDELIERS

1 YEAR POST-DOCTORAL POSITION
(RENEWABLE 1 YEAR)
CENTRE DE RECHERCHE DES CORDELIERS, PARIS, FRANCE

Title: Dent Disease – Evolution and treatments

Job offer: A one year post-doctoral position is available (renewable once), under the supervision of Stéphane Lourdel, in the Gilles Crambert team "Renal physiology and tubulopathies", at the Centre de Recherche des Cordeliers, Paris, France.

The host group explores the cellular and the molecular mechanisms involved in Dent disease type 1, a rare inherited disorder of the proximal tubule characterized by low molecular weight proteinuria, hypercalciuria with nephrolithiasis, and progressive renal failure. The disease is caused by inactivating mutations in the *CLCN5* gene encoding the $2Cl^-/H^+$ exchanger ClC-5. Until now, there is no specific treatment. To understand more precisely the cellular and the molecular mechanisms involved in the physiopathology of Dent Disease type 1, we have generated a *knock-in* (KI) mouse model stably carrying a ClC-5 mutation that belongs to the most frequent class of mutants observed in patients with Dent disease type 1. Our previous investigations using the KI animals demonstrate that mitochondria may play a crucial role in the pathophysiology of Dent Disease type 1. We also demonstrated that the transgenic mice displayed progressive renal inflammation and subsequent fibrosis with aging. In addition, we observed that the KI mice did not gain weight and showed significantly less fat mice then control mice. In addition, these animals displayed a progressive attenuation of glucosuria with age. This suggests a possible switch in their general metabolism and handling of metabolites. Moreover, ClC-5 is expressed in other tissues such as the liver where its function has never been explored previously. As a whole, our project aims at to further investigating the cellular and molecular mechanisms involved in the evolution of Dent disease type 1, and at identifying relevant therapeutic strategies to slow down the progression of this disease. So far, no correlation between genotype and phenotype has been established for patients with Dent disease type 1 as several parameters were not taken into account. Therefore, the postdoc will also aim at studying clinical parameters in close collaboration with the hospital.
For the development of this project, the selected applicant will use *in vivo* and *in vitro* approaches, and will benefit from the strong expertise of the host laboratory in the analysis of the renal phenotype of transgenic mice, and their exploration at the cellular and the molecular levels. An access to state-of-the-art techniques will be provided in the Centre de Recherche des Cordeliers.

Qualifications and experience: Applicants will hold PhD in Physiology and Physiopathology with strong experience in molecular biology, biochemistry and immunohistochemistry. An official approved training for animal experimenting is recommended. Skills in renal pathophysiology would be an asset. The selected candidate should be highly motivated, enthusiastic, independent and team-oriented scientist.

Scientific environment: The laboratory belongs to the “Centre de Recherche des Cordeliers” (www.crcordeliers.fr) located in Paris. In addition to the scientific environment if this institute, the laboratory has access to extensive research core facilities including an animal facility.

Contact: Applicants are invited to send a CV with a list of publications, a summary of research experience, a letter motivation and contact information of referees to stephane.lourdel@sorbonne-universite.fr and elise.decombiens@gmail.com.