Joint Doctorate I-SITE ULNE / KU Leuven in Islet Cell Biology

Location
Lille, France / Leuven, Belgium

Centres
Inserm UMR1190: Translational Research for Diabetes, University of Lille, France
VIB-KU Leuven Center for Brain & Disease Research, Belgium

Supervisors
Caroline Bonner (Lille) and Adrian Liston (Leuven)

Type
Joint doctorate (3 years Lille and 1 year Leuven)

Start Date
October 1, 2018

Description

The Inserm UMR1190: Translational Research for Diabetes, University of Lille and the Autoimmune Genetics Laboratory, Leuven is looking for a skilled and highly motivated PhD student. These internationally recognized research groups are embedded in the infrastructures of the University of Lille and the VIB-KU Leuven and will unite to understand the role of Hepatocyte-Nuclear-Factor 1A (HNF1A) in the regulation of glucose homeostasis. This joint doctorate program is seeking for a skilled and ambitious student with innovative thinking and a certain degree of independence.

In mouse pancreatic islets, HNF1A regulates the expression of the insulin (INS) gene and possibly other hormonal genes along with several other genes linked with insulin secretion, e.g., genes that encode proteins involved in glucose transport such as GLUT2 and glucose metabolism. Mutations in HNF1A cause Maturity-onset-diabetes-of-the-young (MODY) and the most common form is the hepatocyte-nuclear-factor-MODY (HNF1A-MODY). In humans, HNF1A allows insulin to be produced normally in childhood, but the amount of insulin secreted reduces with age, by still unexplained mechanisms. Findings in rodents, suggest that mutations in HNF1A may disrupt the development of beta cells in the embryo, which become dysfunctional in the adult. Others suggest defects in glucose sensing and transport to be the cause.
The general aim of this thesis is to unveil new hypothesizes for the specific function of HNF1A in human islets. The physiological and pathophysiological relevance of our findings will be confirmed *in-vivo* using HNF1A deficient mice versus littermate control mice.

The successful candidate will have a background in islet cell biology & physiology and will work on the biochemical and genetic pathways to better characterize the role

of HNF1A in the regulation of pancreatic hormone gene expression and secretion.

For over a decade Dr. Bonner has been interested in the dysregulations causing the metabolic syndrome (obesity, T2D and MODY), which reveals the intricate nature of glucose and lipid metabolism and the loss-of-function mutations in the transcription factors namely: HNF1A and HNF4A in orchestrating this association. These studies in Lille led to the discovery of SGLT1, SGLT2 and HNF4A expression and function in human adult pancreatic alpha cells, whereby, HNF4A and SGLT2 is required for normal regulation of glucagon (Bonner et al., Nature Medicine, 2015).

Dr. Liston's team has developed a *"beta cell fragility model"* to decipher the variations in the intrinsic fragility or robustness of beta cells, which contribute to the development of diabetes. Dr. Liston also has a strong interest in the discovery of the molecular pathway(s) influencing disease. This is enhanced by his management of two Core Facilities for the University of Leuven - the FACS Core and MutaMouse, a genome engineering facility, which will be hugely beneficial for this PhD thesis project.

Contact:

Dr. Caroline Bonner

Email: caroline.bonner@univ-lille.fr