CNRS UMR 8199

Génomique Intégrative et Modélisation des Maladies Métaboliques

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Fédération de Recherche 3508, LabEx EGID

Lille, 6th of June, 2019.

PhD Fellowships in CNRS UMR8199 – EGID – Université de Lille, Lille, France

The laboratory CNRS UMR8199 "*Génomique intégrative et Modélisation des Maladies Métaboliques*" (Integrated genomics and metabolic diseases modelling, http://www.good.cnrs.fr) offers up to **five** 3-year PhD fellowships designed for outstanding and motivated graduated students of any nationality.

About the environment

By joining the CNRS UMR8199 unit (http://www.good.cnrs.fr), you will be part of a world-class multidisciplinary team dedicated to the identification and characterization of genetic variations and to the molecular mechanisms associated with metabolic diseases such as diabetes, obesity and kidney disease, using latest cutting-edge approaches in genetics, genomics, bioinformatics, biostatistics, molecular and cell biology, and animal models. The research unit counts 60 people headed by Professor Philippe Froguel, MD, PhD. The unit is part of the *Université de Lille*, *Institut Pasteur de Lille* (IPL) and the European Genomic Institute for Diabetes (EGID, http://www.egid.fr) and won recent national and international calls for multimillions euros projects "Laboratory of Excellence renewal" (LabEx EGID2), "Equipment of Excellence" (EquipEx LIGAN-MP), National Center for Precision Diabetic Medicine IHU2 PreciDIAB, ERC, IMI Horizon2020…

Our main research center is located in Lille (Northern France), a very active and attractive city. At the intersection of Brussels, Paris, and London, the city has a strong University of 70,000 students, the largest in France. This university has a vibrant Faculty of Medicine with a comprehensive research pole center where UMR8199 is mainly implanted in the new EGID building since 2017. The UMR8199 is the founder of the LabEx EGID focusing on basic and translational research in diabetes, and comprising 220 researchers and supporting staff from 3 UMRs: UMR8199, UMR1011 directed by Prof Bart Staels, UMR1190 directed by Prof François Pattou). EGID is directed by Prof Philippe Froguel and has been renewed to 2024. EGID research groups share several platforms in genomics, immune phenotyping, human islet preparation and transplantation, and in metabolic phenotyping of animal models (including rodents and minipigs). The UMR8199 is also affiliated to IPL an independent non-profit private foundation created by Louis Pasteur in 1894. IPL is a leading center of excellence in medical research working in active partnership with the University and Hospitals of Lille and research Institutions (Inserm, CNRS). IPL has 6 research units mainly focusing on infectious and inflammatory diseases, neurodegenerative diseases, cardiovascular diseases, metabolic

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diseases, diabetes, obesity, cancer and drug discovery, and 10 state-of-the-art technological platforms ("omics", cell imaging, animal facilities, BSL-2-3, mass spectrometry…) and 6 start-up (see website Annual report*:* *https://www.pasteur-lille.fr/*).

The PhD students joining the UMR8199 through this call will be part of the Lille health PhD program within the Doctoral School "Biology and Health" of Lille. The Doctoral School provides students a stimulating academic environment for advanced multi-disciplinary training in basic biological and biomedical research, applied clinical research, medically-related technological innovations and Public Health research (http://edbsl.univ-lille2.fr/en/welcome.html).

Missions

We propose up to five PhD fellowship positions starting from September 2019 or later according to students' availabilities. Students will integrate one of our world leading teams in the field of diabetes and obesity and will benefit from the expertise of renowned experts in the following areas of research:

- Metabolic functional (epi)genomics and their abnormalities in type 2 diabetes and related disorders

- Molecular pathophysiology of diabetes, obesity and kidney diseases

Students will have the unique opportunity to choose and develop their PhD projects integrating the expertise and platforms of excellence shared by UMR8199 different groups and PIs around (epi)genomics and (patho)physiology. The group is committed to equity and inclusion. All qualified applicants will receive consideration for employment without regard to race, color, religion, gender, gender identity or expression, sexual orientation, national origin, genetics, disability, or age.

PhD projects

Up to 5 PhD positions will be opened under the possible supervision of Dr Amélie Bonnefond, Prof Inga Prokopenko, Dr Fabien Delahaye (team1), or Dr Jean-Sébastien Annicotte, and Dr Régine Chambrey (team2).

Team 1 headed by Dr Amélie Bonnefond is entitled "Metabolic functional (epi)genomics and their abnormalities in type 2 diabetes and related disorders (including obesity, kidney disease, lipids disorders)".

Dr Amelie Bonnefond investigates the contribution of rare genetic variants to the risk of monogenic or common forms of type 2 diabetes or obesity, through integrative studies combining large-scale human genetics/genomics (through several approaches of next-generation sequencing) and functional studies (in various cell models). Via this PhD project, the student will markedly develop skills in next-generation sequencing, cell biology and possibly biostatistics and computer analyses.

Prof Inga Prokopenko scientific interest is in statistical multi-omics method development for dissection of highly-dimensional longitudinal omics data. With the developed methods, her group dissects the pathophysiological processes that contribute to susceptibility to common complex human phenotypes, their heterogeneity and role in the development of comorbid conditions by dissecting various data layers of human large-scale next-generation multi-omics studies. The PhD project will be led by a student with strong background in human molecular genetics, strong

computational skills and knowledge of statistics and epidemiology and will target the role of human obesity in the common types of cancer susceptibility through dissection of obesity heterogeneity through the diverse biological pathways.

Dr Fabien Delahaye is focusing on characterizing the cellular genomic events associated with early exposure and increased risk for age-related diseases combining single-cell technology, genome-wide and *in vitro* functional assays on Hematopoietic Stem and Progenitor Cells (HSPCs). A significant part of the team's effort is dedicated to the development of novel analytical approaches to enable the discovery, from the considerable amount of data generated, of mechanisms involved in disease onset and progression. We are confident that this fellowship represents a unique opportunity to develop essential skills in computational biology.

Team 2 headed by Dr Jean-Sébastien Annicotte dissects the molecular links between insulin producing cells, insulin target tissues and T2D/obesity development.

Dr Jean-Sebastien Annicotte investigates the role of signaling pathways involved in insulin secretion, metabolic homeostasis and tissue dysfunction observed during T2D. His main focus is to develop key models to better understand pancreatic physiology. During the PhD project, we will primarily use complementary and innovative approaches (from mouse models, lineage tracing experiments to genome-wide approaches) to decipher the molecular and cellular mechanisms underlying key activities for the maintenance of the beta-cell identity.

Dr Régine Chambrey leads the research group in renal pathophysiology. Through the development and analysis of different mouse models of kidney disease, Régine Chambrey has acquired a unique expertise in renal disorders modelling in mice. Régine Chambrey is focusing her research project toward chronic kidney failure and its tight link with insulin resistance. This PhD project involves several complementary approaches from the use/generation of normal and genetically or non-genetically engineered mouse models, in vivo phenotyping, histological and immunohistological analyses, multiplex immunoassays to multi-omics screenings for identification of molecular mechanisms involved in the development of the disease.

CVs and application letters should be sent to **Phd-2019@listes.egid.fr**
Deadline: 31/10/19

Relevant publications

- Saeed S *et al*. *Loss of function mutations in ADCY3 cause monogenic severe obesity*. **Nat Genet**. 2018 Feb;50(2):175-179. doi: 10.1038/s41588-017-0023-6.

- Bonnefond A *et al*. *Rare MTNR1B variants impairing melatonin receptor 1B function contribute to type 2 diabetes.* **Nat Genet**. 2012 Jan 29. doi: 10.1038/ng.1053.

- Delahaye F *et al. Sexual dimorphism in epigenomic responses of stem cells to extreme fetal growth.* **Nat Commun**. 2014 Oct 10;5:5187. doi: 10.1038/ncomms6187.

- Wijetunga NA & Delahaye F *et al. The meta-epigenomic structure of purified human stem cell populations is defined at cis-regulatory sequences*. **Nat Commun**. 2014 Oct 20;5:5195. doi: 10.1038/ncomms6195.

- Blanchet E, *et al. E2F transcription factor-1 regulates oxidative metabolism.* **Nat Cell Biol**. 2011 Aug 14;13(9):1146-52. doi:10.1038/ncb2309.

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- Rabhi N, *et al. KAT2B Is Required for Pancreatic Beta Cell Adaptation to Metabolic Stress by Controlling the Unfolded Protein Response.* **Cell Rep**. 2016 May 3;15(5):1051-61. doi: 10.1016/j.celrep.2016.03.079.

- Prelot L, et al. *Machine Learning in Multi-Omics Data to Assess Longitudinal Predictors of Glycaemic Trait Levels.* 2018. **bioRxiv** 358390; doi: https://doi.org/10.1101/358390.

- Fedko I, *et al. Genome-Wide Inferred Statistics for fasting indices of glucose homeostasis – genetic correlation with inflammation markers.* **bioRxiv** 496802; doi: https://doi.org/10.1101/496802.

- Karen I. Lopez-Cayuqueo et al. *A Mouse Model of pseudohypoaldosteronism type II Reveals a Novel Mechanism of Renal Tubular Acidosis*. **Kidney Int***. 2018 Sep;94(3):514-523.* doi: 10.1016/j.kint.2018.05.001.

- Gueutin V et al. *Renal β-intercalated cells maintain body fluid and electrolyte balance*. **J Clin Invest***.* 2013 Oct;123(10):4219-31. doi: 10.1172/JCI63492.

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