CNRS UMR 1283 8199

Epigénomique Intégrative du Diabète et des Maladies Métaboliques

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Fédération de Recherche 3508, Labex EGID

PhD Studentship in CNRS UMR1283/8199 – EGID – Université de Lille, Lille, France

The laboratory CNRS UMR1283/8199 "*Génomique intégrative et Modélisation des Maladies Métaboliques*" (Integrated genomics and metabolic diseases modelling, http://www.good.cnrs.fr) offers up a 3-year PhD studentship designed for an outstanding and motivated graduated student of any nationality.

Missions

We propose a PhD studentship position starting between September and December 2021 or later according to students' availabilities. Students will integrate our new world leading team in the field of bioactivity metabolomics of diabetes, obesity and cardiometabolic diseases and will benefit from the expertise of renowned experts in the following areas of research:

The student will have the unique opportunity to develop their PhD project integrating the expertise and platforms of excellence shared by UMR1283/8199 different groups and PIs around (epi)genomics, metabolomics and (patho)physiology. The Unit is committed to equity and inclusion, and therefore all qualified applicants will receive consideration for employment regardless of race, religion, gender, gender identity or expression, sexual orientation, national origin, genetics, disability, or age.

Supervisors

The project will be supervised by Prof. Marc-Emmanuel Dumas and Dr. Amélie Bonnefond in Team 1 at UMR1283 INSERM / 8199 CNRS.

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, lipid disorders)".

Prof. Marc-Emmanuel Dumas leads the metabolomic activities at UMR1283/8199 and in Team 1, investigating the role of microbial metabolome in cardiometabolic diseases, by combining mass spectrometry, bioinformatics and biological validations through functional assays. In particular Prof. Dumas' group investigates how microbial metabolites inhibit host kinases. He is the director of the joint "Laboratoire Associé International" in Integrative Metabolism between Imperial and Université de Lille.

Dr Amélie 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).

PhD project

The PhD project will focus on developing preclinical assays in animal models, cell-based assays, bioartificial organs in the context of cardiometabolic diseases (obesity, insulin resistance, type 2 diabetes, non-alcoholic fatty liver disease, ischaemic heart disease) with a range of functional "omics", including metabolomics and next generation sequencing (RNAseq, metagenomics, etc…).

The PhD project will include the experimental dissection of the microbiome-host metabolic and signalling crosstalk. More specifically, the PhD student will focus on:

• experimental cell-based assays

• faecal microbiota transplantations and other strategies to modulate the microbiome

• testing the biological activity of microbial metabolites and identifying their signalling targets

• target gene validations in cells and animal models

Via this PhD project, the student will markedly develop skills in next-generation sequencing, cell biology and possibly biostatistics and computer analyses.

Environment

By joining the CNRS UMR1283/8199 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 UMR1283/8199 is mainly implanted in the new EGID building since 2017. The UMR1283/8199 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: UMR1283/8199, UMR1011 directed by Prof Bart Staels, UMR1190 directed by Prof François Pattou). EGID is directed by Prof Philippe Froguel and has been renewed until 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 UMR1283/8199 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 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-ups.

The PhD student joining the UMR1283/8199 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). UMR1283/8199 is also spearheading the joint Imperial College London / Université de Lille Laboratoire Associé International in Integrative Metabolism (Metabol-IC) which will set up a joint PhD program between Lille and London with numerous training workshops, seminars and travel fellowships for research stays at Imperial College London and Université de Lille.

CVs and application letters should be sent to marc-emmanuel.dumas@cnrs.fr
Deadline 31/08/21

Relevant publications

- Brial F, Chilloux J, Nielsen T, Vieira-Silva S, Falony G, Andrikopoulos P, Olanipekun M, Hoyles L, Djouadi F, Neves AL, Rodriguez-Martinez A, Mouawad GI, Pons N, Forslund S, Le-Chatelier E, Le Lay A, Nicholson J, Hansen T, Hyötyläinen T, Clément K, Oresic M, Bork P, Ehrlich SD, Raes J, Pedersen OB, Gauguier D, **Dumas ME.** Human and preclinical studies of the host-gut microbiome co-metabolite hippurate as a marker and mediator of metabolic health. Gut. 2021: gutjnl-2020-323314. doi: 10.1136/gutjnl-2020-323314.
- Brial F, Alzaid F, Sonomura K, Kamatani Y, Meneyrol K, Le Lay A, Péan N, Hedjazi L, Sato TA, Venteclef N, Magnan C, Lathrop M, Dumas ME, Matsuda F, Zalloua P, Gauguier D. The Natural Metabolite 4-Cresol Improves Glucose Homeostasis and Enhances β-Cell Function. Cell Rep. 2020;30(7):2306-2320.e5. doi: 10.1016/j.celrep.2020.01.066.
- Hoyles L, Fernández-Real JM, Federici M, Serino M, Abbott J, Charpentier J, Heymes C, Luque JL, Anthony E, Barton RH, Chilloux J, Myridakis A, Martinez-Gili L, Moreno-Navarrete JM, Benhamed F, Azalbert V, Blasco-Baque V, Puig J, Xifra G, Ricart W, Tomlinson C, Woodbridge M, Cardellini M, Davato F, Cardolini I, Porzio O, Gentileschi P, Lopez F, Foufelle F, Butcher SA, Holmes E, Nicholson JK, Postic C, Burcelin R, **Dumas ME.** *Molecular phenomics and metagenomics of hepatic steatosis in non-diabetic obese women*. Nature Medicine 2018;24(7):1070-1080.
- Baron M, Maillet J, Huyvaert M, Dechaume A, Boutry R, Loiselle H, Durand E, Toussaint B, Vaillant E, Philippe J, Thomas J, Ghulam A, Franc S, Charpentier G, Borys JM, Lévy-Marchal C, Tauber M, Scharfmann R, Weill J, Aubert C, Kerr-Conte J, Pattou F, Roussel R, Balkau B, Marre M, Boissel M, Derhourhi M, Gaget S, Canouil M, Froguel P, **Bonnefond A**. Loss-of-function mutations in MRAP2 are pathogenic in hyperphagic obesity with hyperglycemia and hypertension Nat Med . 2019;25(11):1733-1738. doi: 10.1038/s41591-019-0622-0.
- **Bonnefond A**, Boissel M, Bolze A, Durand E, Toussaint B, Vaillant E, Gaget S, Graeve F, Dechaume A, Allegaert F, Guilcher DL, Yengo L, Dhennin V, Borys JM, Lu JT, Cirulli ET, Elhanan G, Roussel R, Balkau B, Marre M, Franc S, Charpentier G, Vaxillaire M, Canouil M, Washington NL, Grzymski JJ, Froguel P. Pathogenic variants in actionable MODY genes are associated with type 2 diabetes. Nat Metab. 2020;2(10):1126-1134. doi: 10.1038/s42255-020-00294-3.

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- Saeed S, **Bonnefond A**, Tamanini F, Mirza MU, Manzoor J, Janjua QM, Din SM, Gaitan J, Milochau A, Durand E, Vaillant E, Haseeb A, De Graeve F, Rabearivelo I, Sand O, Queniat G, Boutry R, Schott DA, Ayesha H, Ali M, Khan WI, Butt TA, Rinne T, Stumpel C, Abderrahmani A, Lang J, Arslan M, Froguel P. 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.

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