MASTER BIOLOGY and HEALTH SCIENCE of LILLE

Research Projects 2026-2027

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Cellular, Integrative and Translational Neuroscience

Title: **Maternal Obesity as a Disease Modifier in Prader-Willi Syndrome: Dissecting Gene-Environment Interactions**

Mentor: **Sebastien G. BOURET**, Inserm UMR-S 1172, Lille Neuroscience & Cognition Research Center, Lille Neuroendocrinology lab, Tel: 03-5950-7551. E-mail: sebastien.bouret@inserm.fr

Prader-Willi syndrome (PWS) is a rare neurodevelopmental disorder caused by the loss of paternally expressed genes within the chromosome 15q11–q13 locus. Clinically, PWS follows a biphasic trajectory: severe neonatal hypotonia and failure to thrive transition into childhood-onset hyperphagia, impaired energy homeostasis, endocrine dysfunction, cognitive impairment, and maladaptive behaviors culminating in life-threatening obesity. Despite a shared genetic etiology, phenotypic severity varies markedly among affected individuals, suggesting that factors beyond the primary genetic lesion modify disease expression.

Growing evidence indicates that early-life environmental exposures influence long-term metabolic and neurobehavioral outcomes. Maternal overweight and obesity, now affecting up to half of pregnancies in many countries, profoundly alter the intrauterine and early postnatal environment, predisposing offspring to dysregulated appetite control, altered hypothalamic circuit development, and behavioral dysfunction. Strikingly, these alterations overlap with core pathophysiological features of PWS. However, whether maternal obesity modifies the trajectory or severity of PWS phenotypes has never been systematically examined.

We hypothesize that an obesogenic maternal environment synergizes with PWS-associated genetic deficiencies during critical developmental windows to exacerbate metabolic and neurobehavioral dysfunction. To test this hypothesis, we will leverage a novel, translationally relevant mouse model of PWS, the Del Ndn-Magel2 mouse, to determine how maternal diet-induced obesity during gestation and lactation influences offspring growth dynamics, feeding behavior, hypothalamic function, and behavioral phenotypes.

By integrating developmental, metabolic, and neurobehavioral analyses, this project will establish whether maternal obesity functions as a disease modifier in PWS. Defining these gene-environment interactions will advance our mechanistic understanding of phenotypic variability in neurodevelopmental disorders and may identify modifiable maternal risk factors capable of mitigating disease severity in genetically vulnerable populations.

Title: T**argeting Hypothalamic Neuroendocrine Circuits in Polycystic Ovary Syndrome: From Developmental Programming to Novel Pharmacological Approaches**

Tutor: **Paolo GIACOBINI**, Inserm U1172, Equipe: Development and Plasticity of Neuroendocrine Brain. Tel. 0320622060 ; E-mail: paolo.giacobini@inserm.fr

Polycystic Ovary Syndrome (PCOS) is a highly prevalent endocrine and metabolic disorder characterized by hyperandrogenism, ovulatory dysfunction and increased cardiometabolic risk. Abnormal activity of neurons regulating the pulsatile release of Gonadotropin-releasing hormone (GnRH) has been implicated in the neuroendocrine dysfunctions observed in PCOS. However, the mechanisms linking developmental androgen exposure to long-term alterations of hypothalamic networks remain incompletely understood. The objective of this project is to investigate how an aberrant prenatal exposome alters the organization and activity of hypothalamic neuroendocrine circuits controlling reproduction. Using established mouse models of PCOS developed in the laboratory, the student will characterize structural and functional changes in GnRH regulatory networks, including other key hypothalamic populations. The project will combine neuroanatomical approaches (immunohistochemistry and neuronal circuit mapping), molecular analyses of hypothalamic signaling pathways, and physiological assessment of reproductive and metabolic phenotypes. Importantly, the project will also explore innovative pharmacological strategies aimed at restoring normal neuroendocrine function in PCOS models.

Title : **4BL cells : novel mediators of tissue damage in relapsing and progressive Multiple Sclerosis**

Tutor : **Lennart MARS** – Lille Neuroscience & Cognition (UMR-S1172), Group Neuroinflammation and multiple sclerosis, 03.20.62.68.61 – Lennart.Mars@inserm.fr

The last decade has seen remarkable progress in the comprehension and clinical management of Multiple Sclerosis (MS). Undoubtedly an autoimmune disease, MS mobilises the full breath of the innate and adaptive immune response. The complexity of this chronic inflammatory disease goes beyond autoreactivity, implicating immune dysregulation caused by genetic predisposition, progressive immune-senescence and aging, and at the latest stages immune independent neurodegeneration.
We are working on a novel B cell subset that expands in the elderly (>65) and contributes to CD8 immune senescence. Our preliminary data suggests these B cells are augmented in MS patients and blunted by MS treatments. The pathogenic nature of inflammatory B cells, their cellular cross-talk and their pathogenicity are being studied in mouse models of MS.
A motivated M2R student will study the transcriptomic and secretory profile of these cells and address the environmental cues driving the differentiation of 4BL cells and their pathogenicity in animal models.

Title: **Seeding of Tau aggregation and spreading in neurons**

Tutor: **Caroline SMET-NOCCA**, U1167 Inserm RID-AGE - Equipe 3: Déterminants moléculaires de la maladie d'Alzheimer et autres maladies neurodégénératives. Institut Pasteur de Lille, rue Professeur Calmette - +33(0)320877382. caroline.smet-nocca@univ-lille.fr

Inhibition of O-β-linked N-acetylglucosaminyl hydrolase (OGA) is a strategy explored for treating tauopathies, a group of neurodegenerative diseases including Alzheimer's disease (AD), associated with dysfunction of the Tau protein. Together with OGA, O-GlcNAc transferase (OGT) regulates O-GlcNAcylation, a post-translational modification that modulates protein function and interacts with phosphorylation. Increasing O-GlcNAcylation has been shown to stabilize soluble, non-toxic Tau and prevent its pathological aggregation in mouse models. However, a phase 2 clinical trial of an OGA inhibitor failed to meet its primary outcome in early AD patients, who exhibited faster cognitive decline despite reduced Tau pathology, suggesting off-target effects due to the enzyme's pleiotropic activity.
In this project, we aim to develop new tools to selectively enhance Tau O-GlcNAcylation as an alternative to OGA pharmacological inhibition. We have designed nanobody-OGT bifunctional proteins that target Tau via the nanobody specific recognition and increase its O-GlcNAcylation through the OGT catalytic domain. In human iPSC-derived Tau-/- neurons, Tau variants and nanobody-OGTs will be co-expressed to assess their effects on Tau O-GlcNAcylation. We will evaluate their functional impact on Tau spreading and aggregation using microfluidic devices that are culture systems allowing the isolation of neuron synapses and somas in different compartments to specifically address these questions. This strategy may provide a therapeutic alternative to OGA inhibitors by specifically targeting Tau O-GlcNAcylation in neurodegenerative diseases.

Sujet : **Assessing the connection between Alzheimer's disease genetic risk factors PLCG2 and PTK2B in human neurons**

Tuteur : **Julie DUMONT.** UMR 1167 – RID-AGE, Equipe "Déterminant moléculaires de la maladie d'Alzheimer et des syndromes apparentés ». Tel : 03 20 87 73 82 - e-mail : julie.dumont@univ-lille.fr

Alzheimer's disease (AD) is characterized by the accumulation of Aβ, abnormal phosphorylation of tau, and synaptic failure. A high-content screen of 198 AD risk genes in rat primary neuronal cultures identified PLCG2 as a key regulator of synaptic integrity. Rare loss-of-function variants in the PLCG2 gene markedly increase AD risk and impair synaptic structure, elevate Tau phosphorylation and enhance Aβ production in human induced pluripotent stem cell (iPSC)-derived neurons and astrocytes (hiNs/hiAs). We also identified PTK2B, which encodes the Ca^{2+}-dependent kinase PYK2, as a modulator of Tau and amyloid neurotoxicity. Consistently, we characterized an AD-associated PTK2B regulatory variant that alters PYK2 expression and increases phosphorylated Tau and Aβ levels in hiNs/hiAs. Preliminary data suggest that PLCG2 loss-of-function (LoF) modifies PYK2 levels and phosphorylation, indicating a shared Ca^{2+}-dependent pathogenic cascade. We hypothesize that PLCG2 and PYK2 cooperate to drive AD-related synaptic and molecular defects in neurons. Using CRISPR-edited, iPSC-derived neuronal models, microfluidic devices, and multi-omics analyses, we aim to: (i) determine whether PYK2 mediates PLCG2-dependent alterations in APP metabolism, Tau pathology and synaptic structure and function; and (ii) define convergent PLCG2–PTK2B signaling pathways. This project will characterize the PLCG2–PYK2 axis in AD and identify shared, potentially druggable molecular targets that underlie the detrimental impact of these two genetic risk factors in neurons.

Title : **Probing mechanotransduction downstream of synaptic cell adhesion molecules**

Tuteur : **Devrim KILINC** - Inserm U1167, Risk Factors & Molecular Determinants of Aging-related Diseases. 03 20 87 78 01 - devrim.kilinc@pasteur-lille.fr

Chemical synapses of the nervous system form the basis of learning and memory. Their regulation is a key factor in understanding neuropathological processes leading to cognitive decline and dementia. Accordingly, synapse loss due to the disruption of neuronal plasticity mechanisms is an early event in the Alzheimer's disease (AD) pathogenesis (10.1007/s00401-019-02004-0). Synapses undergo activity-dependent structural change, which involves a number of mechanically relevant processes, including cytoskeleton and cell adhesion molecules (CAMs) (doi.org/10.3389/fncel.2018.00483). However, little is known about the mechanical aspects of synaptic plasticity, and if and how AD genetic risk factors are involved therein. Within this framework, this M2 project aims to study the role of mechanotransduction downstream of synaptic CAMs in human induced neurons (hiNs). We will induce pre- and post-synapse formation on axons and dendrites through mechanical stimulation of Amyloid precursor protein (APP) and N-Cadherin (NCad), transsynaptic CAMs, via magnetic tweezers force application in microfluidic devices that fluidically isolate axons and dendrites (doi.org/10.1002/adhm.201600895). Shape change and synaptic protein accumulation will be evaluated via live-cell imaging and immunocytochemistry. In complementary experiments, we will analyze the synaptic localization of APP and NCad as a function of synaptic potentitation and AD-related synaptotoxicity (doi.org/10.1093/braincomms/fcaa139/5898625). This is an ambitious project at the intersection of neurodegenerative diseases and mechanobiology fields that deals with an emerging, yet understudied concept using custom, innovative tools.

Diabetes and Cardio-metabolic diseases

Title: **Transcriptional control of hepatic cell phenotypic plasticity in chronic liver diseases**

Tutor: **Jérôme EECKHOUTE** – INSERM U1011 Récepteurs nucléaires, maladies cardiovasculaires et diabète, Faculté de Médecine de Lille, Pôle Recherche, Bd du Professeur Leclerc, Bâtiment J&K – Tel : 03.20.97.42.19 ; jerome.eeckhoute@inserm.fr

Our team studies the molecular mechanisms that govern liver cell identity and dysfunction in metabolic and chronic liver diseases. We focus on how transcriptional regulation reshapes hepatocyte functionin disease progression toward fibrosis or failure. By integrating functional genomics, multi-omics data mining, and experimental models, we aim to identify key regulatory pathways and therapeutic targets underlying liver plasticity.
The proposed Master 2 internship will explore hepatocyte plasticity at the interface between wet and dry laboratory approaches. The student will combine molecular and cellular experiments with bioinformatic analysis of high-throughput datasets to uncover regulatory mechanisms driving liver cell reprogramming during disease. The project will be carried out within a dynamic, multidisciplinary team of experienced researchers, offering close supervision and hands-on training in both experimental and computational methods.

LiverID team : https://u1011.univ-lille.fr/en/research-topics/theme-4-integrated-transcriptional-analysis-of-liver-diseases

Title: **ECM-Driven Nuclear Mechanisms Governing Epithelial Fate in Liver Disorder**

Tutor: **Rita MANCO** - UMR 1011 INSERM, Laboratoire J&K, Pôle Recherche, Faculté de Médecine, Bd du Pr Jules Leclercq, Lille. rita.manco@inserm.fr

The extracellular matrix (ECM) is a key regulator of epithelial cell behaviour by providing both biochemical and mechanical cues. In the liver, cholangiocytes interact with a laminin-rich basement membrane under physiological conditions, whereas disease is associated with a shift toward collagen- and fibronectin-rich environments. This remodelling is accompanied by increased cellular plasticity, enabling a subset of cholangiocytes to acquire hepatocyte-like features. Preliminary data suggest that these fate transitions are associated with ECM-dependent changes in nuclear mechanics and chromatin organization, indicating that the nucleus acts as a central integrator of microenvironmental signals.
This project employs a multidisciplinary approach, combining advanced 3D culture systems and quantitative imaging, to: i) Characterize how different ECM compositions influence nuclear architecture in human cholangiocytes using immunostaining of nuclear lamins (Lamin A/C, Lamin B1) and high-resolution image analysis; ii) Investigate how mechanical signals are transmitted to the nucleus by analysing cytoskeletal organization and LINC complex components; iii) Determine the role of cytoskeletal tension in shaping nuclear structure through pharmacological perturbations and quantitative imaging readouts.
The central hypothesis is that ECM-dependent mechanical cues regulate cholangiocyte fate by modulating nuclear architecture and stability. Disruption of this mechanotransduction axis may underlie pathological epithelial plasticity observed in chronic liver disease. Insights from this study may open new therapeutic avenues targeting tissue mechanics to control cell fate and liver regeneration.

Title: **Generating and Validating an Inducible SGLT4 Knockout Mouse Model**

Supervisor: **Caroline BONNER** | Inserm U1190, Institut Pasteur de Lille | +33 (0) 32 06 23 413| caroline.bonner@univ-lille.fr

Sodium-glucose cotransporter 4 (SGLT4) is predominantly expressed in the intestinal epithelium and exocrine pancreas and is hypothesised to transport mannose, fructose and other monosaccharides. Our group has previously demonstrated that global Sglt4 knockout mice are resistant to diet-induced obesity, implicating SGLT4 as a key regulator of metabolic homeostasis. However, the temporal and tissue-specific contribution of SGLT4 to this phenotype remains to be established.

This internship aims to generate and validate an inducible global Sglt4 knockout mouse model. Sglt4loxP/loxP mice, in which loxP sites flank exons 4–10 of the Sglt4 locus, will be crossed with rtTA-CMV-Cre mice, in which Cre recombinase expression is controlled by doxycycline-inducible rtTA. The student will implement a three-generation breeding strategy to obtain homozygous Sglt4loxP/loxP::rtTA-CMV-Cre mice in sufficient numbers (target: n = 10 per experimental group). Work will include colony management, systematic genotyping by PCR for both the floxed allele and the Cre transgene, and initiation of Western diet feeding to model diet-induced obesity prior to the induction of Sglt4 deletion.

If mouse numbers permit, the student will participate in a pilot pharmacological study assessing the metabolic impact of our validated anti-SGLT4 monoclonal antibody in Western diet-fed mice. Following a 14-day subcutaneous injection protocol, body composition, fasting glycaemia, and adipose and muscle tissue mass will be assessed at sacrifice, providing first pharmacological proof-of-concept for SGLT4 as a therapeutic target in diet-induced obesity.

This project will provide hands-on training in transgenic mouse genetics, breeding strategies, molecular genotyping, and metabolic disease modelling, within an internationally competitive research programme targeting SGLT4 as a novel therapeutic axis in obesity and metabolic disease.

Title: **Programming Resilient Islets for Type 1 Diabetes**

Tutor: **Isabel GONZÁLEZ MARISCAL** - INSERM UMR1190 Translational Research of Diabetes and Metabolic Disorders, Pôle recherche, place de Verdun, Lille – 03.20.62.34.05 - isabel.gonzalez-mariscal@inserm.fr

Type 1 diabetes (T1D) is an autoimmune disease characterized by the progressive destruction of pancreatic beta cells, affecting approximately 200,000 individuals in France. Although islet transplantation has demonstrated clear advantages over insulin therapy in terms of glycemic control, quality of life, and long-term outcomes, its efficacy remains limited by a substantial loss of grafted islet mass during the peri-transplantation period. This early loss results from a combination of cellular stress, inflammatory responses, and immune-mediated mechanisms that impair islet survival, engraftment, revascularization, and function. Furthermore, transplanted islets remain highly susceptible to environmental stressors, such as dysglycemia, pregnancy, viral infections, and autoimmune recurrence, which can progressively compromise graft performance.

In this context, our research aims to investigate the molecular and cellular mechanisms underlying islet vulnerability and to develop innovative therapeutic strategies to enhance islet resilience. We focus on the integration of pharmacological approaches and synthetic biology tools to dynamically modulate beta cell function and survival. In particular, we are developing engineered islets capable of adapting to environmental stress through the implementation of stress-responsive synthetic promoters, enabling precise temporal control of gene expression.

We propose a Master 2 internship project for a student interested in uncovering the molecular mechanisms of beta cell adaptation and transcriptional regulation, and in contributing to the development of next-generation therapeutic strategies for T1D.

Title: **PPARα and metabolic memory in diabetic retinopathy**

Tutors: **Anna Rita CANTELMO**, **David DOMBROWICZ** - U1011, Récepteurs Nucléaires, Maladies Métaboliques et Cardiovasculaires, Institut Pasteur de Lille, Rue du Professeur Calmette, Lille - Tel: +33 320 87 71 48 - anna-rita.cantelmo@univ-lille.fr

Diabetes mellitus affects an increasing global population, with diabetic retinopathy (DR) and diabetic macular edema (DME) being major causes of vision loss. Endothelial dysfunction plays a pivotal role in DR, where chronic hyperglycemia drives persistent metabolic and epigenetic alterations, contributing to 'metabolic memory' and disease progression.

Peroxisome Proliferator-Activated Receptor α (PPARα) serves as a key regulator at the intersection of metabolism and epigenetics. While primarily involved in lipid metabolism, PPARα also modulates inflammatory responses and influences DNA methylation. In diabetes, its expression is repressed due to hypermethylation, which may contribute to sustained endothelial dysfunction. Notably, PPARα agonists have demonstrated protective effects in DR, raising the question of whether their benefits stem from epigenetic modulation rather than metabolic regulation alone.

This project aims to: (1) assess endothelial PPARα epigenetic alterations as potential markers of vascular dysfunction in diabetes, and (2) investigate the interplay between metabolic and epigenetic pathways via PPARα in retinal endothelial cells. This study seeks to uncover novel endothelial targets for therapeutic intervention in DR.

Title: **Deciphering nuclear receptor-driven endothelial cell plasticity**

Tutor: **Anna Rita CANTELMO** - U1003, Laboratory of Cell Physiology, Cité scientifique, SN3 - Tel: 03 20 33 70 78 - anna-rita.cantelmo@univ-lille.Fr

Endothelial cells (ECs) are highly plastic and can adapt their phenotype in response to environmental and pathological cues. Under conditions such as chronic inflammation or metabolic stress, ECs undergo endothelial-to-mesenchymal transition (EndMT), a phenotypic switch characterized by loss of endothelial identity and acquisition of mesenchymal features.

EndMT contributes to vascular dysfunction and is increasingly recognized as a key driver of cardiovascular diseases, including atherosclerosis and diabetes. Despite sharing similarities with epithelial-to-mesenchymal transition (EMT), the molecular and transcriptional mechanisms regulating EndMT remain incompletely understood.

Nuclear receptors (NRs) are a superfamily of ligand-activated transcription factors that respond to steroid hormones, lipids, and metabolic intermediates. By controlling gene expression programs involved in metabolism, proliferation, and differentiation, NRs play central roles in maintaining cellular homeostasis. Given that ECs are continuously exposed to circulating NR ligands, NRs are ideally positioned to regulate endothelial function and plasticity. However, their contribution to EndMT and endothelial dysfunction remains largely unexplored.

We hypothesize that (some) NRs drive EndMT by regulating key hallmarks of this process, including increased endothelial migration and permeability. To test this hypothesis, we will generate a comprehensive atlas of NR expression at both mRNA and protein levels across multiple in vitro models of EndMT. This approach will allow us to identify candidate NRs associated with endothelial dysfunction. Selected candidates will be functionally validated to determine their role in controlling EC plasticity and barrier integrity.

Overall, this project aims to uncover novel regulatory mechanisms linking NR signaling to EC plasticity and to provide a foundation for the development of innovative therapeutic strategies targeting vascular diseases associated with EndMT.

Title: **Role of the nuclear receptor Rev-erbα in angiogenesis**

Supervisor: **Benoit POURCET**– Université de Lille INSERM U1011 Institut Pasteur de Lille CHU Lille EGID – 01 rue du Pr Calmette – 0320877125 benoit.pourcet@univ-lille.fr

Atherosclerosis is a chronic inflammatory disease of large vessels triggered by the accumulation of cholesterol and leukocytes in the vascular wall. During atherogenesis, vascular wall thickening induces local hypoxia and promotes the vasa vasorum expansion by angiogenesis. These neovessels are however immature and then promote leakage of lipids and leukocytes thus contributing to plaque progression and rupture. The molecular and cellular mechanisms involved in the growth of the perivascular blood network are not known. Reducing its expansion could, however, represent an innovative therapeutic strategy in the treatment of these diseases. Our preliminary data suggest that the nuclear receptor Rev-erb-α controls angiogenesis and intraplaque neovascularization ex vivo and in vivo. This proposal aims to determine the impact of Rev-erb-α in endothelial cells during angiogenesis using in vivo and in vitro approaches. For that purpose, angiogenesis will be assessed in vivo by confocal and light sheet microscopy in endothelial-specific Rev-erbα-/- mice and their control by analyzing the development of the vascular network of newborn retinas. The role of Rev-erb-α on angiogenic processes will then be analyzed in vitro using 3D spheroid models of cell competition. The pathways involved in angiogenesis will be assessed in tissues and cultured cells by WES and RT-qPCR. This M2R proposal aims to determine the impact of Rev-erb-α in angiogenesis during atherosclerosis and to define the molecular and cellular mechanisms involved.

Title: **Role of FAT10/UBD in hepatocyte injury during MASH**

Tutors: **Réjane PAUMELLE-LESTRELIN and Guillaume LASSAILLY** - INSERM- UMR1011 "Nuclear Receptors, Metabolic and Cardiovascular Diseases", Team 1: “Inter-organ communication in cardiometabolic diseases”, J&K Laboratory - Faculty of Medicine, Research Center, Lille - Bd Professor Jules Leclerc, Lille Tel: +33 3 20 97 42 09 rejane.lestrelin@univ-lille.fr

Metabolic dysfunction-associated steatohepatitis (MASH) is a growing cause of cirrhosis and hepatocellular carcinoma, particularly in regions with a high prevalence of obesity and diabetes. Its pathophysiology is based on chronic inflammation and an imbalance Immuno-metabolic processes involving lipotoxicity, oxidative stress, and altered cell survival mechanisms.
The ubiquitin-like protein FAT10 appears to be a potential key regulator involved in protein degradation, energy metabolism, and senescence, but its role in hepatocytes during MASH remains poorly understood. Induced by pro-inflammatory cytokines such as TNFα and IFNγ, FAT10 is also overexpressed in the majority of hepatocellular carcinomas, suggesting a role in tumorigenesis and resistance to apoptosis. However, its functions appear to be context-dependent, with both pro- and anti-apoptotic effects reported.
In this context, this project aims to characterize the molecular pathways modulated by FAT10 in hepatocytes subjected to metabolic stress mimicking MASH, in in vitro and ex vivo cell models.
The analyses will target apoptosis, autophagy, and DNA lesions, endoplasmic reticulum stress and oxidative stress, in order to better understand the role of FAT10 in disease progression and liver carcinogenesis.

Fundamental and clinical oncology

Title: **Modeling Diamond-Blackfan Syndrome in Zebrafish for Personalized Management of Patients Carrying Variants in the RPL17 Gene**

Tutor: **Pierre-Olivier ANGRAND** - Cell Plasticity, Persistence and Metastasis Team, CRCLille, Institut ONCOLille, Univ. Lille, Inserm U1366, CHU Lille, CNRS UMR9020 – pierre-olivier.angrand@univ-lille.fr

Diamond-Blackfan Syndrome (DBS) is a rare congenital disorder characterized by anemia, various malformations, and an increased predisposition to cancer. More than twenty genes are known to be involved in DBS. Recently, the RADEME team (ULR7364, Univ. Lille, CHU Lille) identified a new variant in the RPL17 gene, which encodes a protein of the large ribosomal subunit, in a family of patients with DBS. The internship topic proposes to characterize zebrafish lines generated by the CRISPR/Cas9 system that carry mutations in the rpl17 gene, with two main objectives. The first is to obtain DBS models to better understand the molecular mechanisms of the pathology. The second objective is to develop a functional test to study the pathogenicity of new variants identified clinically in patients carrying mutations in RPL17.

Immunity, Inflammation, Infection

Title : **4BL cells : novel mediators of tissue damage in relapsing and progressive Multiple Sclerosis**

Tutor : **Lennart MARS** – Lille Neuroscience & Cognition (UMR-S1172), Group Neuroinflammation and multiple sclerosis, 03.20.62.68.61 – Lennart.Mars@inserm.fr

The last decade has seen remarkable progress in the comprehension and clinical management of Multiple Sclerosis (MS). Undoubtedly an autoimmune disease, MS mobilises the full breath of the innate and adaptive immune response. The complexity of this chronic inflammatory disease goes beyond autoreactivity, implicating immune dysregulation caused by genetic predisposition, progressive immune-senescence and aging, and at the latest stages immune independent neurodegeneration.

We are working on a novel B cell subset that expands in the elderly (>65) and contributes to CD8 immune senescence. Our preliminary data suggests these B cells are augmented in MS patients and blunted by MS treatments. The pathogenic nature of inflammatory B cells, their cellular cross-talk and their pathogenicity are being studied in mouse models of MS.

A motivated M2R student will study the transcriptomic and secretory profile of these cells and address the environmental cues driving the differentiation of 4BL cells and their pathogenicity in animal models.

Title: **Targeting Carbonyl Stress in Aging: Role of RAGE Antagonists**

Tutor: **Chantal FRADIN**, BioPrev: from inflammaging to prevention. 0320623486, chantal.fradin@univ-lille.fr

Aging is associated with the accumulation of carbonyl stress and the progressive formation of reactive carbonyl species and advanced glycation end products (AGEs), which contribute to cellular dysfunction and the development of age-related pathologies. RAGE (receptor for advanced glycation end products) is a multi-ligand receptor that plays a central role in mediating the deleterious effects of carbonyl stress by amplifying oxidative and cellular stress pathways. Targeting RAGE signalling with specific antagonists may therefore represent an effective anti-stress strategy to limit the impact of carbonyl stress on aging and preserve physiological functions. To test this hypothesis, new RAGE antagonists with improved affinity and inhibitory potential have been synthesised. The aim of the project is to evaluate the protective, anti-stress potential of these compounds in one of the major animal models in ageing biology, the nematode Caenorhabditis elegans. Several transgenic strains expressing human RAGE in different tissues (intestinal, neuronal and muscle) are available to assess whether RAGE antagonists can modulate the onset of ageing hallmarks and promote longevity. Endogenous and/or exogenous ligands such as AGEs and the S100A6 protein will be used to activate RAGE and induce carbonyl stress. A series of physiological assays (locomotion and motility measurements) and molecular analyses (muscle fibre integrity, stress responses and protein homeostasis) will be conducted to determine the impact of RAGE antagonists on stress resistance and ageing.

Title: **Passive microrheology of modified mucus**

Advisor: **Jean-Luc DESSEYN**. U1286/Infinite (CHU de Lille), Group Mucus - jean-luc.desseyn@inserm.fr

The Inserm Unit U1286/Infinte, located on the Lille university hospital campus, is seeking a Master's (M2) candidate for the 2026–2027 academic year. Your profile and interests lie at the interface between biology/biochemistry and biophysics/bioinformatics.
Your project will focus on determining the properties of various mucus samples using passive microrheology, primarily obtained from primary epithelial cell cultures. These studies will be complemented by analyses of bacterial motion. The project mainly involves cell culture as well as computational analysis of the movement of fluorescent beads and bacteria. The objective is to provide proof of concept that selected molecules can modify the properties of altered mucus.
The ideal candidate is meticulous, rigorous, passionate about research, and eager to fully engage in a multidisciplinary project.

Team information: https://lille-inflammation-research.org/en/projects/191-mucus-barrier

Please send your cover letter and CV to: jean-luc.desseyn[at]inserm.fr