2026 – 2027: List of Master 2 internship subjects published by UMR1011

« Bâtiment J&K – Pôle Recherche »

Institut Pasteur de Lille

[Graduate School “Biologie-Santé” de Lille]

[Ecole Graduée Biologie-Santé de Lille]

Deciphering nuclear receptor-driven endothelial cell plasticity

Supervisor: Dr Anna-Rita Cantelmo

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INSERM- UMR1011 "Nuclear receptors, metabolic and cardiovascular diseases"

Team 7: « ENDO-PLAST Role of endothelial cell plasticity and metabolic reprogramming in diseases, Emerging Atip-Avenir team »

Institut Pasteur de Lille – 1 rue du Pr Calmette - Lille

Summary of Master 2 project

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.

Research topics / courses

Diabetes and Cardiovascular diseases

Pparα and metabolic memory in diabetic retinopathy

Supervisor: Dr Anna-Rita Cantelmo

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INSERM- UMR1011 "Nuclear receptors, metabolic and cardiovascular diseases"

Team 7: « ENDO-PLAST Role of endothelial cell plasticity and metabolic reprogramming in diseases, Emerging Atip-Avenir team »

Institut Pasteur de Lille – 1 rue du Pr Calmette - Lille

Summary of Master 2 project

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.

Research topics / courses

Diabetes and Cardiovascular diseases

What is the role of the nuclear receptor Rev-erbα in muscle regeneration during obesity?

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INSERM- UMR1011 "Nuclear receptors, metabolic and cardiovascular diseases"

Team 5: « Nuclear receptors in circadian biology »

Institut Pasteur de Lille – 1 rue du Pr Calmette - Lille

Summary of Master 2 project

Maintaining muscle mass is a major determinant of health due to the central role of skeletal muscle in metabolic regulation, locomotion, and preservation of autonomy. Loss of muscle mass increases dependence and impairs quality of life. Obesity and type 2 diabetes (T2D) are frequently associated with reduced muscle mass and function. This often overlooked complication promotes chronic hyperglycemia, physical inactivity, and worsening obesity. In this context, understanding the cellular and molecular mechanisms responsible for muscle atrophy, fibrosis, and intramuscular lipid accumulation has become a major public health challenge.

Our objective is to identify the determinants governing the fate and function of fibro-adipogenic progenitors, key players in muscle homeostasis, and to assess how these mechanisms are modulated by Rev-erbα, a component of the circadian clock.

We hypothesize that the circadian clock critically regulates the fibroblastic or adipogenic fate of fibro-adipogenic progenitors, as well as their functions in skeletal muscle, thereby influencing muscle mass, regenerative capacity, and the formation of adipocytes within muscle during obesity and insulin resistance.

To test this hypothesis, we will combine a mouse model fed a high-fat diet with analyses of muscle pathophysiology, histology, flow cytometry, and in vivo metabolic assessment using glucose tolerance tests. In the longer term, transcriptomic and molecular analyses will also be performed to elucidate the underlying mechanisms.

Research topics / courses

Diabetes and Cardiovascular diseases

Transcriptional control of hepatic cell phenotypic plasticity in chronic liver diseases

Supervisor: Dr Jérôme Eeckhoute

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INSERM- UMR1011 "Nuclear receptors, metabolic and cardiovascular diseases"

Team 4: "LiverID – Molecular control of pathophysiological alterations to liver cell identifies"

Laboratoire J&K - Département de médecine Pôle Recherche - Bd Pr Jules Leclerc – Lille

Summary of Master 2 project

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 function in 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.

Research topics / courses

Diabetes and Cardiovascular diseases

Characterization of multi-organ injury in acute decompensation of liver cirrhosis (ACLF) in a murine model of intestinal nuclear receptor FXR knockout

Supervisor: Prof. Sophie Lestavel

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INSERM- UMR1011 “Nuclear receptors, metabolic and cardiovascular diseases”

Team 1: “Inter-organ cross talk in cardiometabolic diseases”

Laboratoire J&K - Département de médecine pôle recherche - Bd Pr Jules Leclerc - Lille

Summary of Master 2 project

Acute decompensation of liver cirrhosis (ACLF) is a multi-organ disorder that is life-threatening for patients. It occurs in individuals with advanced liver fibrosis following a sudden triggering event, such as drug exposure or an infectious episode. Given the high mortality rate and the absence of effective treatments, it represents a major public health issue. Unfortunately, existing preclinical models are insufficient.

Recent results from our group show that specific intestinal inactivation of the nuclear receptor Farnesoid X Receptor (intFXR KO) in mice fed a high-fat, high-sugar, and high-cholesterol (HFSC) diet induces chronic liver dysfunction independently of obesity, accompanied by hepatic recruitment of neutrophils (PMNs), a key feature of ACLF.

Based on this distinctive phenotype, the objective of this Master’s thesis internship will be to chemically induce liver fibrosis in intFXR KO mice and to assess whether the HFSC diet leads to decompensation. Validation of this in vivo model will be performed using various techniques based on gene expression analysis, histology, and immunophenotyping. This should ultimately allow the deciphering of the pathophysiological mechanisms involved in organ failure.

Research topics / courses

Diabetes and Cardiovascular diseases

Control of epithelial cell fate by extracellular matrix–dependent nuclear mechanotransduction

Supervisor: Dr Rita Manco

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INSERM- UMR1011 "Nuclear receptors, metabolic and cardiovascular diseases"

Team 8: "Sinusoidal and ECM remodelling in liver diseases, Emerging ATIP-Avenir team"

Laboratoire J&K-Département de médecine Pôle Recherche-Bd Pr Jules Leclerc-Lille

Summary of Master 2 project

The extracellular matrix (ECM) is a key regulator of epithelial cell behavior by providing both biochemical and mechanical signals. In the liver, cholangiocytes normally interact with a basement membrane rich in laminin, whereas pathological conditions are associated with remodeling toward environments enriched in collagen and fibronectin. This remodeling is linked to increased cellular plasticity, allowing a subset of cholangiocytes to acquire hepatocyte-like characteristics. 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 is based on a multidisciplinary approach combining advanced 3D culture systems and quantitative imaging to:

1. characterize the influence of different ECM compositions on the nuclear architecture of human cholangiocytes, using immunostaining of nuclear lamins (Lamin A/C, Lamin B1) and high-resolution image analysis;
2. analyze the transmission of mechanical signals to the nucleus by studying cytoskeletal organization and components of the LINC complex;
3. determine the role of cytoskeletal tension in nuclear structuring using pharmacological perturbations and quantitative imaging measurements.

The central hypothesis is that ECM-dependent mechanical signals regulate cholangiocyte fate by modulating nuclear architecture and stability. Disruption of this mechanotransduction axis may underlie the pathological epithelial plasticity observed in chronic liver diseases. The expected results could open new therapeutic perspectives targeting tissue mechanical properties to control cell fate and liver regeneration.

Research topics / courses

Diabetes and Cardiovascular diseases

Role of Fat10/UBD in hepatocyte suffering during MASH

Supervisor: Prof. Réjane Paumelle Lestrelin / Dr Guillaume Lassaily (U1190)

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INSERM- UMR1011 "Nuclear receptors, metabolic and cardiovascular diseases"

Team 1: "Inter-organ cross talk in cardiometabolic diseases"

Laboratoire J&K-Département de médecine pôle recherche-Bd Pr Jules Leclerc-Lille

Summary of Master 2 project

Metabolic dysfunction–associated steatohepatitis (MASH) is an increasingly common cause of cirrhosis and hepatocellular carcinoma, particularly in regions with high prevalence of obesity and diabetes. Its pathophysiology is driven by chronic inflammation and an immunometabolic imbalance involving lipotoxicity, oxidative stress, and impaired cellular survival mechanisms.

FAT10 protein, a ubiquitin-like protein, 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 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 exposed to metabolic stress mimicking MASH, using in vitro and ex vivo cellular models. The analyses will focus on apoptosis, autophagy, DNA damage, endoplasmic reticulum stress, and oxidative stress, in order to better understand the role of FAT10 in disease progression and hepatic carcinogenesis.

Research topics / courses

Diabetes and Cardiovascular diseases

Role of the nuclear receptor Rev-erbα in angiogenesis

Supervisor: Dr Benoit Pourcet

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INSERM- UMR1011 "Nuclear receptors, metabolic and cardiovascular diseases"

Team 5: « Nuclear receptors in circadian biology »

Institut Pasteur de Lille – 1 rue du Pr Calmette - Lille

Summary of Master 2 project

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.

Research topics / courses

Diabetes and Cardiovascular diseases

Role of type 2 innate lymphoid cells in skeletal muscle homeostasis

Supervisor: Prof. Yasmine Sebti

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INSERM- UMR1011 “Nuclear receptors, metabolic and cardiovascular diseases”

Team 5: « Nuclear receptors in circadian biology »

Institut Pasteur de Lille – 1 rue du Pr Calmette - Lille

Summary of Master 2 project

Skeletal muscle is an essential metabolic organ, responsible for the uptake of nearly 75% of blood glucose in the postprandial state. One of the distinctive features of skeletal muscle is its remarkable ability to regenerate following damage caused by intense exercise or injury. This process requires precise spatiotemporal interactions between muscle stem cells, fibro-adipogenic progenitors, and immune cells, which together provide the optimal microenvironment for stem cell proliferation and differentiation.

Innate lymphoid cells (ILCs) have been identified as a subset of leukocytes, subdivided into three groups, that play essential roles in maintaining tissue homeostasis. Type 2 ILCs (ILC2s) are highly plastic cells that exhibit a tissue-specific transcriptional signature allowing them to adapt to their microenvironment. To date, their role in skeletal muscle remains poorly understood. Our preliminary data show infiltration of ILC2s into skeletal muscle of wild-type mice following injury. Moreover, mice deficient in ILC2s display increased fibrosis and an impaired immune response after injury compared to controls. We therefore hypothesize that ILC2s contribute to muscle repair processes and metabolic adaptation.

This project aims to (1) characterize the role of ILC2s in muscle homeostasis and regeneration, and (2) identify their molecular signature in regenerative and pathological contexts using single-cell RNA sequencing approaches. With this proposal, we aim to shed light on how the physio-pathological context of muscle determines ILC2 identity and how this muscle-specific molecular signature influences their function

Research topics / courses

Diabetes and Cardiovascular diseases