CMD InnoCARE (Innovation pour les maladies CArdiovasculaires, métaboliques et REspiratoires)

Master 2 Internship proposal (2024-2025)

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Profile(s) linked to the project:
☒ Experimental Biology *(Recherche expérimentale)*
☐ Research and Biological Data Analysis *(Recherche et analyse de données biologiques)*
☐ Clinical Research *(Recherche clinique)*

Lab: l'institut du thorax

Team: II – Pr Benjamin Lauzier

Name and position of the supervisor: Eva Guilloteau and Benjamin Lauzier

Email of the supervisor: eva.guilloteau@univ-nantes.fr; benjamin.lauzier@univ-nantes.fr

Candidate (if known):

Title of the internship: **Is paediatric cardiac hypertrophy due to altered vascularization caused by gestational diabetes-induced hyper-O-GlcNAcylation?**

Summary of the internship proposal:
Gestational diabetes (GD) is a specific form of diabetes that develops during pregnancy and results in impaired foetal development. O-GlcNAcylation (O-GlcNAc), a post-translational modification is increased in diabetic mother, in cardiomyocyte hypertrophy in both rat neonatal cardiac cells and an adult mouse model and in the placenta of DG mother. But, chronic O-GlcNAc increase in diabetes is considered deleterious. It has been shown that an increase in O-GlcNAc associated with maternal hyperglycaemia could be a major determinant in the alteration of vascularization and in the development of paediatric cardiac pathologies. Vascular endothelial growth factor (VEGF) plays a central role in these processes. In physiological conditions, VEGF establishes good vasculogenesis and is necessary to induce the production of nitric oxide (˙NO) by eNOS., acting as a relaxing factor. During GD, hyperglycaemia acts as a pro-angiogenic, pro-constrictor, pro-coagulant, pro-inflammatory and pro-permeability agent. VEGF/eNOS balance is altered. **We suppose that the increase in O-GlcNAc level in heart of baby from DG could be an important determinant of vascular remodelling leading to the development of cardiac pathology reported in neonatal patient delivered from diabetic mother.** We will explore the impact of protein hyper-O-GlcNAcylation on cardiac and placental development and its vascularization with a specific rodent model. We will perform analysis on embryo at different days of embryonic life, in order to observe the potential disturbances at different embryonic stages. Specific pathways induced in vascularization and angiogenesis (VEGF, NO pathway, ROS markers, permeability markers) will be analysed by microscopy, Western-Blot, O-GlcNAcylomic. A particular interest will be focused on the effect of hyper-O-GlcNAcylation, and vascular remodelling using immunohistology, western blot, cell culture.