

**CMD InnoCARE (Innovation pour les maladies
Cardiovasculaires, métaboliques et REspiratoires)**
Master 2 Internship proposal (2024-2025)
1 page maximum



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: Benjamin Lauzier

Email of the supervisor: Benjamin.lauzier@univ-nantes.fr

Candidate (if known):

Title of the internship: Exploration of the link between Pediatric Cardiac Hypertrophy and O-GlcNAcylation

Summary of the internship proposal:

Between **13 to 44% of pediatric cardiac hypertrophy (PCH)** cases are **linked to poorly managed diabetes**, yet the **exact mechanism leading to PCH is not clearly identified**. Some studies suggest that alterations in glucose metabolism are associated with profound change in insulin dependent signaling pathways. Also, **hyperglycemia is linked to an increase in O-GlcNAcylation (O-GlcNAc) level and aberrant cell proliferation**. This dynamic post-translational modification affects 5000 proteins and is involved in several cellular processes such as cell division and growth, stress response and **transcriptional/translational regulation**. In collaboration with Pr. Luc Bertrand from Brussels (Partner 5), we have demonstrated using a rat model that an **increase in O-GlcNAc levels is associated with cardiomyocyte hypertrophy**. We have also demonstrated, with Dr Tarik Issad (Partner 2) that cardiac O-GlcNAc levels are tightly regulated during post-natal development. However, further research is needed to assess if an increase in O-GlcNAcylation associated with hyperglycemia during pregnancy causes long-term effects on cardiac structure and function.

Hypothesis: While neonatal cardiac hypertrophy associated to gestational diabetes has long been considered as the consequence of fetal hyperinsulinemia, **we hypothesize that the increase in O-GlcNAc levels associated with hyperglycemia is an important pathogenic factor of cardiac hypertrophy found in infants delivered from diabetic mothers.**

Through OMICS analysis, cell biology and molecular biology the candidate will define how hyper-O-GlcNAcylation is involved in cardiac development.