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 – groupe Cardiac physiology and pharmacology

Name and position of the supervisor: Manon Denis, PH

Email of the supervisor: denis.manon89@gmail.com

Candidate (if known):

Title of the internship: Role de la O-GlcNAcylation dans la survie des patients cyanogènes

Summary of the internship proposal:

My working hypothesis is the following: Levels of O-GlcNAc remain high after birth, acting as a protective mechanism, hence: high levels of O-GlcNAc is a central process for the survival of young patients suffering from hypoxic condition associated with cardiac malformation.
Considering that increase in O-GlcNAc levels is beneficial in acute situation of hypoxemia such as septic shock or hemorrhagic shock and that O-GlcNAc plays such a pivotal role in cell survival, we will evaluate the potential link between the remarkable survival of cyanotic congenital heart disease patients and their high levels of O-GlcNAc. Through this project, I should unravel new pathways or mechanisms playing a key role in the resistance to hypoxemia.
O-GlcNAc is a post-translational modification (PTM) described in 1984 by Hart and Torres, affecting intracellular proteins (or intracellular part for transmembrane proteins) and involved in almost all cellular process, from transcription to regulation of enzymatic function. To date, more than 8,000 Human proteins have been described as O-GlcNAcylated. This modification happens on serine and threonine; thus, it can compete with phosphorylation in some situation. However, unlike phosphorylation, which is regulated by multiple phosphatases and kinases, O-GlcNAcylation is only dependent on two enzymes: O-GlcNAc transferase (OGT), which adds the GlcNAc moiety, and O-GlcNAcase (OGA), which removes it. O-GlcNAcylation is extremely well preserved between species (from plant to superior mammals), and is so fundamental to life that animals knock out for the key enzymes in the process (OGT or OGA) die in utero or very quickly after birth respectively.
We will explore using molecular and cellular biology, and functional study in sample from patient how high O-GlcNAc level can protect them from the cyanogenic situation.
The student will take part in the cardiomyocyte isolation and all the study of the functional adaptation through pharmacological approach and WB, qPCR, pulldown…