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: Inserm U1087, l'institut du thorax

Team: Team 3

Name and position of the supervisor: Sarah Beck-Cormier

Email of the supervisor: sarah.beck@univ-nantes.fr

Title of the internship: Characterisation of a new mouse model for the Primary Familial Brain Calcification disease

Summary of the internship proposal:

The genetic disorder PFBC (primary familial brain calcification) is a rare neurological disorder associated with psychiatric and motor symptoms and characterised by calcium phosphate deposits in the cells of the neurovascular unit, with a major impact on quality of life. Despite the discovery of seven genes responsible for PFBC, current knowledge of the mechanisms by which cerebral calcification is induced remains limited, representing a major obstacle to the development of preventive and therapeutic strategies. Of the three genes most frequently mutated in patients, two, SLC20A2 and XPR1, are highly expressed in brain vascular cells and allow the import (SLC20A2) or export (XPR1) of phosphate.
We have been working on the Slc20a2-/- mice, known to be a good model for PFBC, for several years. Recently, thanks to the Rare Diseases Foundation, we have generated a new mouse model carrying the *Xpr1* gene mutation most frequently found in PFBC patients. The aim of this internship is to characterise this model. To this end, the candidate will assess and quantify the progression of cerebral vascular calcification by using microtomography and histomorphometry techniques. The phosphocalcic homeostasis of this model will also be assessed by biochemical and hormonal assays and by analysing the expression of genes and proteins regulating phosphate homeostasis in the kidney, bone and intestine. Finally, he/she will characterise the environment of the neurovascular unit at the time of the appearance of calcifications by 3D immunofluorescence analyses on thick brain slices, labelling mural cells, endothelial cells, astrocytes, microglia and osteogenic cells.
This work is part of a major project that aim to elucidate the molecular and cellular mechanisms involved in this rare and poorly understood genetic disease and to identify new avenues for drug development.