CMD InnoCARE (Innovation for CArdiovascular, metabolic and REspiratory diseases)

Master 2 Internship proposal (2026-2027)

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

Lab: l'institut du thorax, U1087
Team: Human Genetic (Team 1)

Name and position of the supervisor:
Dr. Salam Idriss, Researcher

Research Group Leader: Prof. Betty Gardie

Email of the supervisor: salam.idriss@univ-nantes.fr

Candidate (if known): To be recruited

Title of the internship: Circadian Regulation of Hepatic Erythropoietin Expression in Human iPSC-Derived Hepatocyte Models

Summary of the internship proposal:
Erythropoietin (EPO) is the master hormone regulating red blood cell production and systemic oxygen homeostasis. While EPO is predominantly produced by the liver during fetal development and by the kidney in adulthood, our recent studies have demonstrated that hepatic *EPO* expression can be reactivated in specific pathological contexts. However, the mechanisms regulating hepatic *EPO* expression remain poorly understood.
Interestingly, renal EPO production and circulating EPO levels exhibit circadian oscillations, suggesting an interaction between oxygen-sensing pathways and the molecular clock. Whether hepatic *EPO* expression is also under circadian control remains unknown.

The objective of this internship is to investigate the circadian regulation of hepatic *EPO* expression using human induced pluripotent stem cell (iPSC)-derived hepatocyte-like cells (HLCs). The student will work with an established differentiation protocol developed in the laboratory and will perform synchronization experiments using circadian entrainment protocols (e.g., dexamethasone treatment). Samples collected over a 48-hour period will be analyzed by RT-qPCR to monitor the expression of *EPO* and key circadian clock genes (*BMAL1, PER1*, *PER2*, *CRY1*, and *REV-ERBα*), and later validated by 3'SRP. Depending on progress, the student may also participate in transcriptomic data analysis.

The project will provide training in stem cell culture, hepatocyte differentiation, molecular biology techniques (RNA extraction, RT-qPCR…), and experimental design for time-series studies. The internship will contribute to ongoing research aiming to uncover novel mechanisms controlling hepatic EPO production and oxygen homeostasis.