Formulaire de stage (sur une page maximum)
Parcours M2 GGBS 2023-24

Laboratoire : **Unité de recherche de l'institut du thorax**, Inserm UMR 1087/CNRS UMR 6291
N° d'équipe : Equipe de Génétique Médicale, Thématique des "Erythrocytoses héréditaires" (Betty Gardie).
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Titre du stage : **Molecular and Functional Characterization of Erythropoietin Mutations Identified in Patients with Hereditary Erythrocytosis**

Résumé du projet proposé:

Our laboratory works on the hypoxia signalling pathway that governs cellular adaptation in response to decreased oxygen availability (**hypoxia**). Indeed, impaired regulation of this pathway has been tightly linked to several pathologies such as **hereditary erythrocytosis (HE).** HE is an inherited condition characterized by an increased number of red blood cells (erythrocytes) which is mainly linked to the overexpression of **erythropoietin (EPO)**.

Recently, our team has identified novel germline mutations in the *EPO* gene in patients with HE. Our preliminary results showed that these novel mutations are targeting fundamental **regulatory elements in the *EPO* gene** which is thus affecting its expression and function.

The aim of this project in general, and internship in particular, will be to depict the epigenetic status of *EPO* locus in the presence and absence of the newly identified mutations, through **pioneering high-throughput assays** such as ATAC-Seq (Assay for Transposase-Accessible Chromatin followed by high-throughput sequencing), ChIP-seq (Chromatin immunoprecipitation followed by sequencing), and CUT&RUN (Cleavage Under targets and release using nuclease).

This study will be conducted using a highly-pertinent **cellular models (2D and 3D)** of the pathology, these models are currently set up in the laboratory. These cellular models rely on the generation of **EPO-producing cells differentiated from patient's-derived induced pluripotent stem cells (iPS**).

In this internship, the student will learn to culture iPS cells and differentiate them into EPO-producing cells and perform different molecular and functional assays.

Options à laquelle est associée ce projet :

☐ Biothérapies de l'appareil locomoteur
X Cardiovasculaire et Facteurs de Risque
X Immunologie-Cancérologie
☐ Immuno-Intervention, Transplantation et Auto-Immunité
☐ Maladies infectieuses
☐ Physiopathologies de l'axe cerveau-intestin