Internship proposition 2026-2027

Master 2 GP Medicine 4R (Repair, Replace, Regenerate, Reprogram)

Lab: TaRGeT UMR1089 Translational Research in Gene Therapy
Team: Génétique Humaine

Name and position of the supervisor: Frédéric Ebstein (CRCN Inserm, Group Leader), Sandra Mercier (PU-PH, CHU Nantes)

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Candidate (if internship filled):

Title of the internship: Deciphering the cellular and developmental consequences of FAM111B and ubiquitin-proteasome system (UPS) dysfunction in human iPSC models.

Summary of the internship proposal:
Our research group has recently described POIKTMP, a rare genetic disorder caused by pathogenic variants in FAM111B, a gene encoding a trypsin-like serine protease.
Affected individuals typically present with a distinctive set of dermatological features, including erythema, telangiectasia, and areas of both hyperpigmentation and hypopigmentation, resulting in a mottled skin appearance. However, the molecular and cellular mechanisms underlying disease pathogenesis remain poorly understood. Recently, we have shown that FAM111B functionally interacts with some components of the ubiquitin-proteasome system (UPS) including proteasome subunits [1].
This project will investigate the cellular consequences of FAM111B and UPS dysfunction during development using human induced pluripotent stem cell (iPSC)-based models. Particular attention will be given to identifying tissue-specific and developmental stage-specific mechanisms that may compensate for impaired FAM111B/UPS function. Ultimately, the project aims to uncover therapeutic targets and pathways capable of restoring proteostasis or mitigating downstream cellular consequences of FAM111B/UPS dysfunction.
The candidate will gain hands-on experience in stem cell biology and translational research in the field of rare genetic disorders.

[1] Vignard V, Maillasson M, Bigot A, Küry S, Besnard T, Broly M, et al. Ubiquitin-proteasome system dysregulation in FAM111B-related poikiloderma and phenotypic spectrum expansion: new case reports and long-term follow-up. EBioMedicine 2025;119:105864. https://doi.org/10.1016/j.ebiom.2025.105864.

Profile(s) linked to the project:

X Experimental Biology *(Recherche expérimentale)*
☐ Clinical Research *(Recherche clinique)*
☐ Research in data analysis (Recherche en analyse de données)