Master Biologie Moléculaire et Cellulaire 'BMC',
Université Paris Cité - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
https://master2bdc.ijm.fr/
Fiche de Projet de Stage de M2, 2026-2027

Unité INSERM ou CNRS ou Université : Inserm U1134, Université de Paris **Intitulé Equipe :** Biologie Intégrée du Globule Rouge-Physiologie du Globule Rouge Normal et Pathologiqque **ED d'appartenance :** ED562-BioSPC **Responsable de l'Equipe :** Pr Laurent Gouya, Sophie Lefevre	**Responsable du Stage :** **Contacts** Adresse : INSERM UMRS_1134 149, rue de Sevres, Hôpital Necker, Bat Lavoisier, 1er Etage, 75015 Paris Email : melanie.franco@inserm.fr Tel : +33 6 45 66 09 99

Titre du projet : Study of proteostasis dysfunction during aging and pathologies in red blood cells and progenitors

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

Proteostasis is all cellular mechanisms involved in protein quality control and is essential during **erythroid differentiation** as well as throughout the lifespan of **red blood cells** (RBCs). Disruption of proteostasis (proteasomal and/or autophagy-lysosomal pathways) leads to the accumulation of damaged or misfolded proteins, promoting protein aggregation, cellular stress, and premature aging. These processes are particularly critical during erythropoiesis, which is characterized by extensive proteome remodeling, and in mature RBCs, which are unable to synthesize new proteins or renew their organelles but must cope with prolonged oxidative stress.

Diseases associated with mutations in the **GBA1** gene represent highly relevant models for studying proteostasis dysfunction. Homozygous GBA1 mutations cause **Gaucher disease**, a lysosomal storage disorder characterized by severe impairment of lysosomal function, while heterozygous mutations constitute a major risk factor for neurodegenerative diseases such as **dementia with Lewy bodies**. In these contexts, failure of protein degradation pathways promotes the accumulation of altered proteins and disrupts cellular aging mechanisms.

This project aims to investigate how proteostasis deregulation during erythroid differentiation and RBC aging contributes to protein accumulation, cellular dysfunction, and protein release under both physiological and pathological conditions. The study will rely on human samples, erythroid cellular models, and targeted perturbations of major proteostasis pathways.

The internship student will actively participate in this multidisciplinary project by contributing to experimental analyses and gaining practical training in cell biology (cell culture, in vitro erythropoiesis, flow cytometry, imaging flow cytometry) and biochemistry (SDS-PAGE and Western blotting, proteostasis activity assays), within a translational research framework involving teams specialized in hematology (U1134, BIGR) and neurodegenerative diseases (U1144, TRANSAND).

Publications de l'équipe relatives au projet de stage (max 5)

1. Gaubert S, et al., Neurosci Biobehav Rev. 2022.
2. Dupuis, L., et al., J Cell Mol Med, 2020.
3. Franco, M., et al., Am J Hematol, 2020.
4. Reihani, N., et al., Haematologica, 2016.
5. Franco, M., et al., Blood, 2013.