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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage de M2, 2022-2023

Unité INSERM ou CNRS ou Université : U 1016 INSERM **Intitulé Equipe : Hématopoïèse Normale et Pathologique** **ED d'appartenance : HOB** **Responsable de l'Equipe : Fontenay/ Bouscary**	**Responsable du Stage : Evelyne LAURET** **Contacts** Adresse : Institut Cochin - 22 rue Méchain 75014 Paris Email : evelyne .lauret@inserm.fr Tel : 06 82 25 19 15

Titre du projet : Role of the DDX6 helicase in normal hematopoiesis

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)
Hematopoiesis includes all the processes/mechanisms involved in the formation of blood cells from the hematopoietic stem/progenitor cell compartment (HSPC). The expression of genes involved in hematopoiesis is regulated at several levels: transcriptional (genetic and epigenetic) and post-transcriptional **(stability and/or translation of transcripts)** regulation. The latter, which includes all controls targeting transcripts, has long been neglected but is crucial because it allows fine regulation and rapid modification of the final protein expression. RNA binding proteins (RBPs) are key players in post-transcriptional regulation. Here we focus on the RBP **"DEAD box RNA helicase DDX6"** which can unwind/rearrange their secondary structures. DDX6 contributes to global mRNA storage, translational repression and/or degradation. A recent work has shown that loss of DDX6 by knockdown (KD) strongly disrupts the commitment between self-renewal and differentiation in various stem cell populations (embryonic and some adult stem cells); this disruption involves translational deregulation of differentiation regulators and modification of chromatin structure (1). To date, no study has focused on the role of DDX6 in the differentiation of normal HSPCs.
The project is part of a **global evaluation of the role of the DDX6 in the regulation/deregulation of normal human hematopoiesis. The objectives are double: 1/ Evaluation of the role of DDX6 in normal hematopoiesis; 2/ deciphering its mechanisms of action.** Our first results acquired through the use of RNA-interference strategies show that DDX6 exerts an important role in HSPC functions where it **controls the balance between self-renewal and differentiation.** Moreover, it also plays a major function in hematopoiesis by being **essential for erythrocyte and megakaryocyte differentiation.**
The proposed Master 2 project aims at confirming our first results and at identifying the mechanisms of action of DDX6 on the commitment of hematopoietic progenitors to the erythroid and megakaryocytic lineages.
1/Stefano, B. D. et al. The RNA Helicase DDX6 Controls Cellular Plasticity by Modulating P-Body Homeostasis. Cell Stem Cell 1–31 (2019)

Publications de l'équipe relatives au projet de stage (max 5)
Poirault-Chassac S., Nivet-Antoine V., Houvert, A, Kauskot, A, Lauret, E, Lai-Kuen, R., Dusanter-Fourt, I.*, and Baruch D.*. Mitochondrial dynamics and reactive oxygen species initiate thrombopoiesis from mature megakaryocytes. Blood Adv 5, 1706–1718 (2021). *co senior authors
Bonnet C., Gou, P., Girel, S., Bansaye, V., Lacout, C., Bailly, K., Schlagetter, MH., Méléard, S.*, and Lauret E.*, Giraudier S.*. Multistage hematopoietic stem cell regulation in the mouse: A combined biological and mathematical approach. Iscience 24, 103399 (2021). *co senior authors
Naudin C, Hattabi A, Michelet F, Miri-Nezhad A, Benyoucef A, Pflumio F, Guillonneau F, Fichelson S, Vigon I*, Dusanter-Fourt I*, Lauret E*. PUMILIO/FOXP1 signaling drives expansion of hematopoietic stem/progenitor and leukemia cells. Blood. 2017 May 4;129(18):2493-2506. *co senior authors.

1 page maximum SVP !