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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : **Intitulé Equipe : Hématopoïèse normale et pathologique** **ED d'appartenance : HOB** **Responsable de l'Equipe : Michaela Fontenay**	**Responsable du Stage : Evelyne Lauret** **Contacts Evelyne Lauret** Adresse : Institut Cochin 22 rue Méchain 75014 Paris Email : evelyne.lauret@inserm.fr Tel : 01 40 51 64 05

Titre du projet : Roles of the FOXP1 transcription factor in the development of normal and leukemic myeloid progenitors

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

FOXP1, originally discovered in B lymphomas, belongs to the Forkhead Factor (Fkh) superfamily, many members of which contribute to the development of various cell types. FOXP1 regulates the self-renewal of embryonic stem cells. Its constitutive deletion is lethal in mice by abnormalities in cardiac development; its inducible deletion reveals that FOXP1 regulates the development of B and T lymphocytes. However, the activities of FOXP1 in CSPH and AML are as yet unexplored. We have established that FOXP1 participates in **the maintenance of CSPH and in the growth of acute myeloid leukemia** (AML) in humans (**Naudin et al, Blood 2017**) through the regulation of their **oxidative stress** (**Oussous et al., in preparation**).

The Master's 2 work that we are proposing is part of the general study of the role of FOXP1 in hematopoiesis and myeloid leukemogenesis. For this purpose, we have Foxp1f/f mice that we crossed with the Vav-iCRE mice to generate animals characterized by a invalidation of the Foxp1 gene in CSPH and therefore hematopoiesis. Our first results show that the hematopoiesis of these mice is disturbed with an expansion of the multipotent myeloid progenitors at the expense of the number of hematopoietic stem cells, leading to a reduction in the potential for hematopoietic reconstitution. In addition, aged mice display a leukemic phenotype. We propose here to **analyze the leukemogenic properties of FOXP1 *in vivo* and *in vitro*.** For this, we will transform the FOXP1fl/fl ;Vav-iCRE mouse CSPHs with the oncogenes MLL-ENL, MLL-AF9 and FLT3-ITD. We will perform methylcellulose cultures of these cells to assess their growth potential *in vitro* in response to the absence of FOXP1. We will also inject these cells into syngeneic mice to assess the impact of FOXP1 on tumor growth *in vivo*.

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

Catelain C, Michelet F, Hattabi A, Poirault-Chassac S, Kortulewski T, Tronik-Le Roux D, Vainchenker W, Lauret E. The Notch Delta-4 ligand helps to maintain the quiescence and the short-term reconstitutive potential of haematopoietic progenitor cells through activation of a key gene network. Stem Cell Res. 2014 Nov;13(3 Pt A):431-41.

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.