Formulaire de stage (sur une page maximum)

Parcours M2 GGBS 2019-20

Laboratoire : CRTI - UMR1064 INSERM, Nantes

Intitulé/N° d’équipe : 1

Nom-Prénom de l’encadrant : CHIFFOLEAU Elise

Courriel de l’encadrant : Elise.Chiffoleau@univ-nantes.fr

Candidat pressenti : Aucun

Titre du stage :

**Epigenetic modulation of mouse dendritic cells following C-type lectin-like receptor-1 triggering.**

C type Lectin-like Receptors (CTLR) represent subtypes of Pattern Recognition Receptors (PRRs) expressed mostly by myeloid cells that can be triggered by self-proteins to fine-tune regulate homeostasis and T cell immunity in sterile inflammation. We demonstrated in both rodent and human that the C-type lectin-like receptor-1 (CLEC-1) acts as an inhibitory receptor in myeloid cells (Thebault, 2009) (Lopez Robles, 2017). We showed in dendritic cells (DC) that CLEC-1 is enhanced by the immunosuppressive cytokine TGFbeta and prevent IL12p40 expression and downstream Th1 and Th17 responses.

In this project, we aim to investigate the role of CLEC-1 in DCs by investigating epigenetic modification following both PRRs activation and CLEC-1 triggering. Indeed, epigenetics has been pivotal in our understanding of how immune cells develop and adapt to different environments. In our Team, J Poschmann has developed an approach based on histone acetylation (H3K27ac) (ChipSeq) to discover epigenetic alterations in response to environmental changes, genetic variation and diseases. H3K27ac allows the identification of both active promoters and enhancers, so we aim to employ this approach to reveal the gene regulatory mechanisms of dendritic cells in response to CLEC-1 triggering by comparing dendritic cells from Wild type and Clec1a deficient mice.

-The first aim of this master 2 will be to discover epigenetic changes in these subpopulations in different conditions of immune regulation.

-In the second aim, we will validate and characterize the gene regulatory mechanisms using functional studies to gain mechanistic insights.

In the long term, a better understanding of the genomics of CLEC-1 in dendritic cells may help to discover new target for immune-modulation in physio/pathology.

- Thebault P., N. Lhermite, G. Tilly, L. Le Texier, T. Quillard, M. Heslan, I. Anegon, J. P. Soulillou, S. Brouard, B. Charreau, M. C. Cuturi and E. Chiffoleau (2009). "The C-type lectin-like receptor CLEC-1, expressed by myeloid cells and endothelial cells, is up-regulated by immunoregulatory mediators and moderates T cell activation." J Immunol 183(5): 3099-3108.

- Lopez Robles M-D., A. Pallier, V. Huchet, L. Le Texier, S. Remy, C. Braudeau, L. Delbos, A. Moreau, C. Louvet, C. Brosseau, P-J Royer, A. Magnan, F. Halary, R. Josien, M-C Cuturi, I. Anegon and E. Chiffoleau. Cell-surface C-type lectin-like receptor CLEC-1 dampens dendritic cell activation and downstream Th17 responses. Blood Advances 2017 1:557-568