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 : Institut Cochin (Inserm U1016/CNRS UMR8104/Paris Descartes) **Intitulé Equipe:** Epigénétique et organisation nucléaire dans la recombinaison et le développement **Responsable de l'Equipe :** Julie Chaumeil	**Responsable du Stage :** Julie Chaumeil / Delphine Ndiaye-Lobry **Contacts** Adresse : 24 rue du Fg St Jacques, 75013 Paris Email : julie.chaumeil@inserm.fr Tel : 01 44 41 24 57

Titre du projet : Generation and analysis of transgenic cell lines to study the role of **nuclear organization** in the regulation of gene expression and **V(D)J recombination** during lymphocyte differentiation.

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)
Although modulation of **chromatin and nuclear organization** are tightly linked to the establishment and maintenance of cell-type specific transcription profiles, as well as the **regulation** of essential processes like DNA recombination and repair, the functional relationships remain unclear. In **lymphocytes**, **V(D)J recombination** is the key-process by which the virtually infinite diversity of antigen receptors is created to combat the equally vast array of antigens. These programmed rearrangements have the potential to generate genomic instability as rounds of cleavage and joining occur every day in millions of B and T cells, and even a tiny error rate can lead to translocations underlying leukemia and lymphomas. Few processes have provided more insights into the fine regulation of locus accessibility. However, the functional role of the changes in chromatin and nuclear landscapes correlated with the initiation and regulation of recombination is still largely unknown. We explore this key question using a combination of single-cell analyses to genome-wide approaches, during embryonic stem cell differentiation towards lymphoid lineages.

The Master project will be essentially based on molecular and cell biology techniques, including cloning, generation of transgenic cell lines and ES cell culture, RNA/DNA in situ hybridization, immunostaining, 3D microscopy, FACS. Some genome-wide "chromosome conformation capture" approaches may also be generated, and analyzed as a collaborative project. In order to study the functional role of nuclear and chromatin environments on antigen-receptor gene expression and V(D)J recombination, the experimental strategy is based on the tagging of the Tcra/d locus to allow its visualization and the tethering / targeting of different nuclear and chromatin proteins in the context of embryonic stem cells differentiated into the lymphoid lineages. In this context, the Master project will consist in the generation and/or analyses of some of these cell lines.

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

· Benbarche S, Lopez CK*, Salataj E*, Thirant C, Laiguillon MC, Aid Z, Lecourt S, Antonini M, Pardieu B, Petit A, Puissant A, **Chaumeil J***, Mercher T*, Lobry C*. **(2019)** BioRXiv ***(*Co-senior authors)***

· Souyris M, Cenac C, Azar P, Daviaud D, Canivet A, Grunenwald S, Pienkowski C, **Chaumeil J**, Mejia JE, Guéry JC. **(2018)** *TLR7* escapes from X chromosome inactivation in immune cells. ***Science Immunology*, 3**, eaap8855.

· Proudhon C, Hao B, Raviram R, **Chaumeil J**, Skok JA. Long-Range Regulation of V(D)J Recombination. ***Adv Immunol*, 128:123-82. (2015)**

· **Chaumeil J**, Micsinai M, Ntziachristos P, Roth DB, Aifantis I, Kluger Y, Deriano L, Skok JA. RAG2 C-terminus and ATM control RAG activity to limit the number of potential translocation substrates. ***Nature Comm*, 31;4:2231. (2013)**

· **Chaumeil J,** Micsinai M, Ntziachristos P, Deriano L, Wang JMH, Ji Y, Nora E, Rodesch MJ, Jeddeloh JA, Kluger Y, Aifantis I, Schatz DG, Skok JA. Higher-order looping and nuclear organization of antigen receptor loci facilitates targeted RAG cleavage and regulated rearrangement in recombination centers. ***Cell Reports,* 3(2):359-370. (2013)**