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, 2025-2026

Unité INSERM ou CNRS ou Université : U101- UMR 8104 **Intitulé Equipe :** Épigénétique et fonctions nucléaires dans les maladies humaines **ED d'appartenance :** ED562 **Responsable de l'Equipe :** Benoit Miotto & Julile Chaumeil	**Responsable du Stage :** Katia Ancelin et Julie Chaumeil **Contacts** Adresse : INSTITUT COCHIN 24, rue du Faubourg Saint-Jacques 75014 Paris, France Email : katia.ancelin@inserm.fr; julie.chaumeil@inserm.fr Tel : +33 1 44 41 24 57

Titre du projet : Investigating chromatin remodelers in X chromosome inactivation escape in the immune system

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)
Biological sex influences physiological differences between males and females and the prevalence of many diseases, including cancers and autoimmune disorders. Recent studies have recognize the genetic impacts of **sex chromosomes** (XX or XY) on these differences. In female mammals, **X-chromosome inactivation (XCI)** silences one of the two Xs to balance **gene dosage** with males. However, in certain tissues or pathological conditions, XCI can become eroded, leading to weakening of gene silencing, allowing some gene to "escape" inactivation. The biological consequences of this double gene dosage remain poorly understood, but could play important role in diseases.
Chromatin regulators, particularly those modulating histone post-translational modifications, are key players in establishing and maintaining XCI, yet their precise roles in loss of XCI remain unclear. The immune system exhibits strong sex-biases in normal and disease conditions, making it a valuable model to study XCI dynamics.
This project aims to investigate how **chromatin remodelers** contribute to **XCI escape at specific immune-related genes** such as Tlr7. Using a unique transgenic mouse model, we will screen for 'epigenetic drugs' (**epidrugs**) to identify factors that modulate XCI escape. By analyzing alveolar macrophages from male and female mice across different ages, we will dissect the regulatory mechanisms governing XCI dynamics and their implications for immune system homeostasis, in health and diseases.

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

Altered X-chromosome inactivation of the TLR7/8 locus and heterogeneity of pDCs in systemic sclerosis.
Du Y, Faz-Lopez B, Ah Kioon MD, Cenac C, Pierides M, Lakin KS, Spiera RF, **Chaumeil J**, Truchetet ME, Gordon JK, Guéry JC, Barrat FJ. J Exp Med. 2025 Mar 3;222(3):e20231809. doi: 10.1084/jem.20231809.

X chromosome regulation and female functional specificities: Are two Xs better than one?].
Chaumeil J✉ , Morey C✉ . Med Sci (Paris). 2024 Dec;40(12):935-946. doi: 10.1051/medsci/2024179.PMID: 39705564

TLR8 escapes X chromosome inactivation in human monocytes and CD4+ T cells.
Youness A, Cenac C, Faz-López B, Grunenwald S, Barrat FJ, **Chaumeil J**, Mejía JE, Guéry JC.
Biol Sex Differ. 2023 Sep 18;14(1):60. doi: 10.1186/s13293-023-00544-5. PMID: 37723501

Collombet S, Ranisavljevic N, Nagano T, Varnai C, Shisode T, Leung W, Piolot T, Galupa R, Borensztein M, Servant N, **Fraser P**✉ **,** **Ancelin K**✉ **,** **Heard E**✉ . Parental-to-embryo switch of chromosome organization in early embryogenesis. *Nature*, **2020**. doi 10.1038/s41586-020-2125-z ✉ Co senior et co pour correspondance

TLR7 escapes X chromosome inactivation in immune cells.
Souyris M, Cenac C, Azar P, Daviaud D, Canivet A, Grunenwald S, Pienkowski C, **Chaumeil J**, Mejía JE, Guéry JC.
Sci Immunol. 2018 Jan 26;3(19):eaap8855. doi: 10.1126/sciimmunol.aap8855. PMID: 29374079