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 : **Université Paris Cité** **Intitulé Equipe : Biologie Fonctionelle Adaptative, equipe EnDF** **ED d'appartenance : BioSpc** **Responsable de l'Equipe :** **Jamileh Movassat**	**Responsable du Stage :** **L'HOTE David** **Contacts** Adresse : 4, rue MA Lagroua Weill-Hallé 75205 Paris cedex 13 Email : david.lhote@u-paris.fr Tel : **0157278404**

Titre du projet :

Epigenetic Regulation of Gonadotrope Cell Differentiation: Role of ISL1 and CHD7 in ERα-Mediated Gene Activation

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

The reproductive function in vertebrates is tightly controlled by pituitary **gonadotrope cells**. During embryogenesis, the specification of the gonadotrope lineage is initiated by the transcription factor **NR5A1**. Our previous work demonstrated that Nr5a1 gene expression is driven by a novel enhancer regulated by **estrogen receptor alpha (ERα)** (Pacini et al., 2019). **Pioneer factors**, a recently discovered class of transcription factors, can bind to condensed chromatin and increase its accessibility, enabling the recruitment of other TFs like ERα. Although they are crucial for cell differentiation, only a few pioneer factors have been identified to date.

The goal of this project is to identify pioneer factors involved in **gonadotrope lineage specification** and to understand the epigenetic mechanisms controlling this process. Using RNA-seq and ChIP-seq, we characterized the ERα cistrome in immature gonadotrope cells. Additionally, BioID experiments allowed us to map the ERα interactome. Integrating these datasets, we identified two promising candidates: ISL1 – a transcription factor known to act as a pioneer factor in other contexts and CHD7 – a histone chaperone implicated in syndromic hypogonadotropic hypogonadism.

The student will investigate the roles of **ISL1** and **CHD7** in regulating ERα activity in αT3-1 cells, a model of immature gonadotrope cells. The project will involve:

1. Validation of protein interactions: Confirm the interaction between ISL1, CHD7, and Erα. 2. Gene disruption studies: Use CRISPR-Cas9 and CRISPRi to inhibit Isl1 and Chd7 expression. 3. Functional analysis: Assess the impact on ERα target genes using qPCR. 4. Epigenetic profiling: Examine changes in ERα binding, histone marks, and chromatin accessibility at target enhancers using ChIP-qPCR and ATAC-qPCR.

This project will enhance our understanding of the epigenetic regulation of gonadotrope cell differentiation and potentially identify a novel pioneer factor. It will also provide new insights into ERα-dependent mechanisms of cell differentiation, opening avenues for further research in developmental and reproductive biology.

Techniques Involved: RNA-seq, ChIP-seq, Co-IP, CRISPR-Cas9, CRISPRi, qPCR, ChIP-qPCR, ATAC-qPCR, cell culture.

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

1: Pacini V, Petit F, Querat B, Laverriere JN, Cohen-Tannoudji J, L'hôte D. Identification of a pituitary ERα-activated enhancer triggering the expression of Nr5a1, the earliest gonadotrope lineage-specific transcription factor. Epigenetics Chromatin. 2019 PMID: 31391075

2: Le Ciclé C, Pacini V, Rama N, Tauszig-Delamasure S, Airaud E, Petit F, de Beco S, Cohen-Tannoudji J, L'hôte D. The Neurod1/4-Ntrk3-Src pathway regulates gonadotrope cell adhesion and motility. Cell Death Discov. 2023 PMID: 37658038