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, 2026-2027

Unité INSERM ou CNRS ou Université : Institut Jacques Monod, UMR7592 et ERL1340 INSERM **Intitulé Equipe : Human neurodevelopment and disorders** **ED d'appartenance : BioSPC** **Responsables de l'Equipe : Vanessa RIBES et Stéphane NEDELEC**	**Responsable du Stage : Claire Dugast-Darzacq/Pascale Gilardi-Hebenstreit** **Contacts :** Adresse : 15 rue Hélène Brion 75013, PARIS Email : **claire.dugast@ijm.fr** Tel : 01 57 27 81 93

Titre du projet : Rewriting the Epigenome: How Distinct PAX3 Fusion Proteins Shape Tumor Heterogeneity

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

Our internship project investigates the **genome remodeling capabilities** of chimeric transcription factors created by chromosomal translocations. These unique fusions combine the DNA-binding domain of PAX3 with the C-terminal regions of various **chromatin regulators**, including transcription factors like FOXO1 and WWTR1 (TAZ), chromatin remodelers such as INO80D, and transcriptional coactivators like NCOA1/2 and MAML3. These PAX3-X fusion proteins are strongly associated with **sarcomas** that exhibit striking **clinical and molecular heterogeneity**. A key question we aim to address is whether each fusion protein establishes a distinct chromatin and transcriptional state early on, thereby shaping tumor identity and diversity.

To explore this, the intern will work with a **cutting-edge pluripotent stem cell-derived organoid model**, where PAX3 fusion proteins are expressed during differentiation. This system allows us to study how these oncogenic factors reprogram transcriptional and chromatin landscapes during cell fate decisions. The project will implement state-of-the-art approaches including **RNA-seq** and **CUT&Tag** to profile transcriptional and chromatin states, as well as immunostaining and **advanced imaging techniques** to assess differentiation, tissue organization, and potential transdifferentiation events.

In parallele this intern will investigate the effects of overexpression of fusion proteins involving PAX3 on the **development of the neural tube in the chicken embryo**, an accessible experimental model in which the effects of PAX3-FOXO1 have already been characterized. Using immunolabeling techniques on histological sections, They will analyze: i) the proliferative state of cells, ii) the organization of the neuroepithelium, iii) cell morphology, iv) the organization of the extracellular matrix, as well as v) the expression of markers of neural differentiation and sarcomas.

Positioned at the **intersection of developmental biology, cancer research, and transcriptional regulation**, this interdisciplinary project offers a unique opportunity to uncover how **oncogenic fusion proteins** hijack developmental programs to **generate tumor heterogeneity**.

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

R. Rondon, et al., *PLOS Biol.* **23**, e3003448 (2025).
TGW Graham et al., Mol Cell. Aug 7;85(15):2854-2868 (2025).
L. Manceau, et al., *PLOS Genet.* **18**, e1009782 (2022).
S. Chong, et al., *Mol. Cell* **82**, 2084-2097 (2022).
S. Chong, C. et al., *Science* **361**, eaar2555 (2018).