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 : UMR7592, Université Paris Cité, CNRS **Intitulé Equipe :** Neurodéveloppement humain et pathologies associées **ED d'appartenance :** BioSPC **Responsable de l'Equipe :** Vanessa Ribes et Stéphane Nédélec	**Responsable du Stage : Claire DUGAST** **Contacts** Adresse : IJM / 15 rue Hélene Brion / 75013 Paris Email : claire.dugast@ijm.fr Tel : Tel :01 57 27 81 93

Titre du projet : ***Illuminating the Transcriptional Switch of PAX3 and PAX7***

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

We are looking for motivated students to join an exciting and cutting-edge project at the intersection of stem cell biology, developmental neuroscience, and live-cell imaging.

Our team uses **organoids** - 3D models of the spinal cord derived from mouse pluripotent stem cells - to recreate early developmental processes in a dish. These organoids offer a unique opportunity to study how cells make fate decisions in a context that closely mimics real tissues.

The project focuses on two key transcription factors, **PAX3** and **PAX7**, which are essential for shaping the sensory dorsal part of the spinal cord. Although these proteins are well-known regulators of gene expression, we still don't fully understand how their activity switches between gene activation and repression in real time, and how this is linked to cell fate decisions.

To go beyond traditional genomic methods, we're implementing advanced *live imaging techniques*, including **FRAP** (Fluorescence Recovery After Photobleaching) and **Single Particle Tracking**, to visualize the dynamic behavior of these transcription factors inside the nuclei of living cells. These approaches allow us to witness in real time i) the rapid binding and unbinding of transcription factors to DNA, ii) their local enrichment into hubs and iii) their mode of diffusion within the nuclear space, offering insights into how their mobility and interactions with chromatin and their co-regulators are regulated during development and could impact cell fate.

By combining cutting-edge microscopy with powerful organoid models, this project provides a unique opportunity to explore the **real-time mechanisms of gene regulation** in a living developing system.

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

-Robin Rondon, Théaud Hezez, Julien Richard Albert, Bernadette Drayton-Libotte, Gloria Gonzalez-Curto, Frédéric Relaix, Claire Dugast-Darzacq, Pascale Gilardi-Hebenstreit, Vanessa Ribes. *Dual PAX3/7 transcriptional activities spatially encode spinal cell fates through distinct gene networks* **BioRxiv 2025** doi: 10.1101/2025.03.11.64266

-Chong,S., Dugast-Darzacq, C., Liu, Z., Dong, P., Dailey, G., Cattoglio, C., Banala, C., Lavis, L., Darzacq, X., Tjian, R. *Imaging dynamic and selective low-complexity domain interactions that control gene transcription*. **Science. 2028.** Jul 27;361(6400).

-Boehning* M, Dugast-Darzacq* C, Rankovic* M, Hansen AS, Yu T, Marie-Nelly H, McSwiggen DT, Kokic G, Dailey GM, Cramer P, Darzacq X, Zweckstetter M. *RNA polymerase II clustering through carboxy-terminal domain phase separation.* **Nat Struct Mol Biol. 2018** Sep;25(9):833-840. **(* co-premier auteur).**

- Divergent transcriptional and transforming properties of PAX3-FOXO1 and PAX7-FOXO1 paralogs. Manceau L, Richard Albert J, Lollini PL, Greenberg MVC, Gilardi-Hebenstreit P, Ribes V.. **PLoS Genet.** 2022 May 23;18(5):e1009782.

- BMP4 patterns Smad activity and generates stereotyped cell fate organization in spinal organoids. Duval N, Vaslin C, Barata TC, Frarma Y, Contremoulins V, Baudin X, Nedelec S, Ribes VC. **Development.** 2019 Jul 25;146(14):dev175430. doi: 10.1242/dev.175430.