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, 2024-2025

Unité INSERM ou CNRS ou Université : UMR7592 **Intitulé Equipe : Cell Cycle & Development** **ED d'appartenance : BioSPC** **Responsable de l'Equipe : Lionel PINTARD**	**Responsable du Stage : Lionel PINTARD** **Contacts** Adresse : 15 rue hélène Brion Email : lionel.pintard@ijm.fr Tel : 01.57.27.80.89

Titre du projet : Deciphering the mechanisms regulating nuclear envelope remodeling during cell division and development

Résumé du Projet de Stage

This project aims to understand **how the cell cycle machinery orchestrates nuclear envelope remodeling** (nuclear envelope breakdown and reformation) and **how this remodeling impacts chromosome segregation and cell division in a developmental context.**

The early *C. elegans* embryo provides a unique and powerful model for studying nuclear envelope dynamics during cell division and development with exquisite spatial and temporal resolution. In the *C. elegans* zygote, the maternal and paternal genomes are initially located in separate pronuclei, surrounded by a nuclear envelope. After pronuclei meeting and juxtaposition, coordinated disassembly of the pronuclei envelopes promotes the mingling of the parental chromosomes on the metaphase plate. In particular, the formation of a membrane scission event between the pronuclei is required for the parental chromosomes to mingle on the metaphase plate and be unified after mitosis. All these events require extensive membrane remodeling orchestrated by the cell cycle machinery, particularly the Polo-like kinase PLK-1 (Martino et al., 2017).

In this context, the main objective will be to dissect how the nuclear envelope is remodeled to allow the unification of the parental genomes after the first mitosis. Specifically, the master student will dissect the molecular mechanisms orchestrating nuclear envelope disassembly by dissecting the role of the mitotic Polo-like kinase PLK-1 in this process using various approaches. We previously reported that PLK-1 is dynamically recruited to the nuclear envelope in prophase (Martino et al., 2017)to trigger lamina depolymerization disassembly of nuclear pore complexes (Nkombo Nkoula et al., 2023), and possibly regulating other substrates at the NE. Indeed, we have identified novel potential PLK-1 targets at the NE using innovative phosphoproteomic approaches (Velez-Aguilera et al., 2024) that we will characterize.

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

Velez-Aguilera, G., Ossareh-Nazari, B., and **Pintard, L**. (2024). Dissecting the Multiple Functions of the Polo-Like Kinase 1 in the C. elegans Zygote. Methods Mol Biol *2740*, 63-88.

Nkombo Nkoula, S., Velez-Aguilera, G., Ossareh-Nazari, B., Van Hove, L., Ayuso, C., Legros, V., Chevreux, G., Thomas, L., Seydoux, G., Askjaer, P., and **Pintard, L**. (2023). Mechanisms of nuclear pore complex disassembly by the mitotic Polo-like kinase 1 (PLK-1) in C. elegans embryos. Sci Adv *9(29)*, eadf7826.

Tavernier, N., Thomas, Y., Vigneron, S., Maisonneuve, P., Orlicky, S., …, Sicheri, F., and Pintard, L. (2021). Bora phosphorylation substitutes in trans for T-loop phosphorylation in Aurora A to promote mitotic entry. Nat Commun *12(1)*, 1899.

Velez-Aguilera, G., Nkombo Nkoula, S., Ossareh-Nazari, B., Link, J., Paouneskou, D., Van Hove, L., Joly, N., Tavernier, N., Verbavatz, J. M., Jantsch, V., and **Pintard, L**. (2020). PLK-1 promotes the merger of the parental genome into a single nucleus by triggering lamina disassembly. Elife *9*, e59510.

Martino, L., Morchoisne-Bolhy, S., Cheerambathur, D. K., Van Hove, L., Dumont, J., Joly, N., Desai, A., Doye, V., and **Pintard, L**. (2017). Channel Nucleoporins Recruit PLK-1 to Nuclear Pore Complexes to Direct Nuclear Envelope Breakdown in C. elegans. Dev Cell *43(2)*, 157-171.e7.