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

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| **Unité INSERM ou CNRS ou Université :**<br>Institut Jacques Monod –<br>UMR7592 CNRS - Université Paris Cité<br><br>**Intitulé Equipe :** Fonctions non-conventionnelles des pores nucléaires<br><br>**ED d'appartenance : BioSPC**<br><br>**Responsable de l'Equipe : Valérie DOYE** | **Responsable du Stage :**<br>Valérie DOYE<br><br>**Contacts**<br>Adresse : Bâtiment Buffon, labo 342-344B<br>15 rue Hélène Brion – 75013 Paris<br><br>Email : valerie.doye@ijm.fr<br><br>Tel : 01 57 27 81 39 |

**Titre du projet : Use of iPSC-derived organoids to characterize nucleoporin mutations causing neurological and kidney disorders**


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

**Nuclear pore complexes** (NPCs) are massive protein assemblies that mediate the trafficking between the cytoplasm and the nucleus. Despite the universal role of NPCs in all nucleated cells, some of their constituents (**nucleoporins**, Nups) are linked to human hereditary diseases affecting specific cell types and organs. However, the underlying molecular mechanisms causing the **pathologies** are often unresolved. In most instances, it is unclear whether a given mutation affects the assembly or transport capability of the NPCs or a non-conventional function of the mutated nucleoporin (in cell cycle, gene regulation or genome integrity) at, or outside of, the nuclear pore. This project aims to functionally analyze mutations in structural nucleoporins that cause steroid resistant nephrotic syndrome (SRNS) a fatal kidney disease in children. To mimic these pathology-causing situations, the M2 student will use **human induced pluripotent stem cells (h-iPSCs)** bearing pathological mutations within one of these structural Nups (collaboration with C. Antignac and G. Mollet – Imagine Institute). He.she will differentiate the mutant and appropriate control iPSC lines towards **3D brain and/or kidney organoids and 2D neurones and/or podocytes** and will combine quantitative imaging and molecular biology approaches to determine how a specific NUP mutation affects, possibly in a cell- or tissue-specific manner, NPC assembly, nuclear transport, and/or gene expression. The project will thus address a fundamental cell biological question on nucleoporin function within and outside NPCs and how mutations in these proteins affect cellular function and differentiation. At the same time, it will contribute to the characterization of the molecular basis of diseases, an essential step towards future targeted therapeutic interventions.


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


- Taniguchi R, Orniacki C, Kreysing JP, Zila V, Zimmerli CE, Böhm S, Turoňová B, Kräusslich HG, **Doye V*,** Beck M*. (2025). *Nuclear pores safeguard the integrity of the nuclear envelope.* ***Nat Cell Biol****.* doi: 10.1038/s41556-025-01648-3.
- Dultz E, **Doye V**. (2025) *Opening the gate: Complexity and modularity of the nuclear pore scaffold and basket.* ***Curr Opin Cell Biol.*** 92:102461. doi: 10.1016/j.ceb.2024.102461. PMID: 39826239
- Orniacki C, Verrico A, Pelletier S, Souquet B, Coulpier F, Jourdren L, Benetti S, **Doye V.** (2023) *Y-complex nucleoporins independently contribute to nuclear pore assembly and gene regulation in neuronal progenitors.* ***J Cell Sci.*** 136(11):jcs261151. doi: 10.1242/jcs.261151.
- Gonzalez-Estevez, A., Verrico, A., Orniacki, C., Reina-San-Martin B., Doye V. (2021*) Integrity of the short arm of nuclear pore Y-complex is required for mouse embryonic stem cell growth and differentiation.* ***J. Cell Sci.***134:jcs258340. doi: 10.1242/jcs.258340.
- Cianciolo Cosentino C., Berto A, Hari M, Loffing J, Neuhauss SCF, Doye V. (2019). *Moderate Nucleoporin 133 deficiency leads to glomerular damage in zebrafish* ***Sci Rep.*** 9:4750. doi: 10.1038/s41598-019-41202-4.