Master Biologie Moléculaire et Cellulaire 'BMC',
Université Paris Cité - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
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Fiche de Projet de Stage de M2, 2026-2027

Unité INSERM ou CNRS ou Université : Institut Jacques Monod (CNRS/Université Paris Cité) **Intitulé Equipe :** Biogenèse des ARN et homéostasie du génome **ED d'appartenance :** BioSPC (Université Paris Cité) **Responsable de l'Equipe :** Benoit PALANCADE	**Responsable du Stage :** Benoit PALANCADE **Contacts** Adresse : Institut Jacques Monod – 15, rue Helene Brion 75013 PARIS Email : benoit.palancade@ijm.fr Tel : 01 57 27 80 39

Titre du projet : Nuclear pore complexes as novel regulators of R-loop-associated genome instability

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

RNA moieties can get incorporated into genomic DNA during transcription, when the nascent transcript anneals back to its template, forming a three-stranded **R-loop**, i.e. a DNA:RNA hybrid and a displaced single-stranded DNA. When accumulating, such R-loops are highly detrimental for genome functions, disturbing **gene expression** and triggering **DNA damage**. Consistently, abnormal R-loop dynamics have been associated with various human diseases, from cancer to neurological disorders. However, the molecular and cellular bases of R-loops harmful impact remain incompletely understood.

Over the last years, our lab has explored the factors regulating R-loop-induced **genome instability**, combining mechanistic characterization in **budding yeast** with experimental validations in **human cells** [1-4]. More recently, we have developed dedicated genetic and proteomic screens, which have revealed novel players in R-loop regulation, including **nuclear pore complexes** (NPCs, [3-4]). Intriguingly, beyond their canonical role in **nucleocytoplasmic exchanges**, NPCs have been involved in genome organization, expression and stability, through yet-to-be explored mechanisms.

Building on these findings, this M2/PhD project will aim to (i) characterize NPCs as novel regulators of R-loops, (ii) unravel the associated molecular and cellular mechanisms, and (iii) ultimately, assess their relevance in pathological situations displaying intrinsic deregulation of R-loop homeostasis. For this purpose, the M2/PhD trainee will use a multidisciplinary panel of experimental strategies: **genetics** (construction and manipulation of yeast mutants [1;3-4]); **molecular biology/-omics** (genomic mapping of R-loops [4]); **biochemistry** (*in vitro* analysis of R-loop resolution [4]); **imaging** (live localization of R-loops with respect to NPCs; nucleocytoplasmic transport assays [3,5]). This project is expected to shed light onto novel conserved regulations modulating R-loop toxicity, paving the way to understanding their pathological implications.

More information about the project and the host lab are available upon request.

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

[1] Bonnet et al., Mol Cell 2017; doi.org/10.1016/j.molcel.2017.07.002
[2] Rombaut et al., Nature Communications 2024; doi.org/10.1038/s41467-024-46547-7
[3] Penzo et al., Nature Communications 2023; doi.org/10.1038/s41467-023-41345-z
[4] Mangione et al., Nature Communications 2025; doi: 10.1038/s41467-025-57588-x
[5] Lautier et al., Mol Cell. 2021; doi: 10.1016/j.molcel.2021.03.030