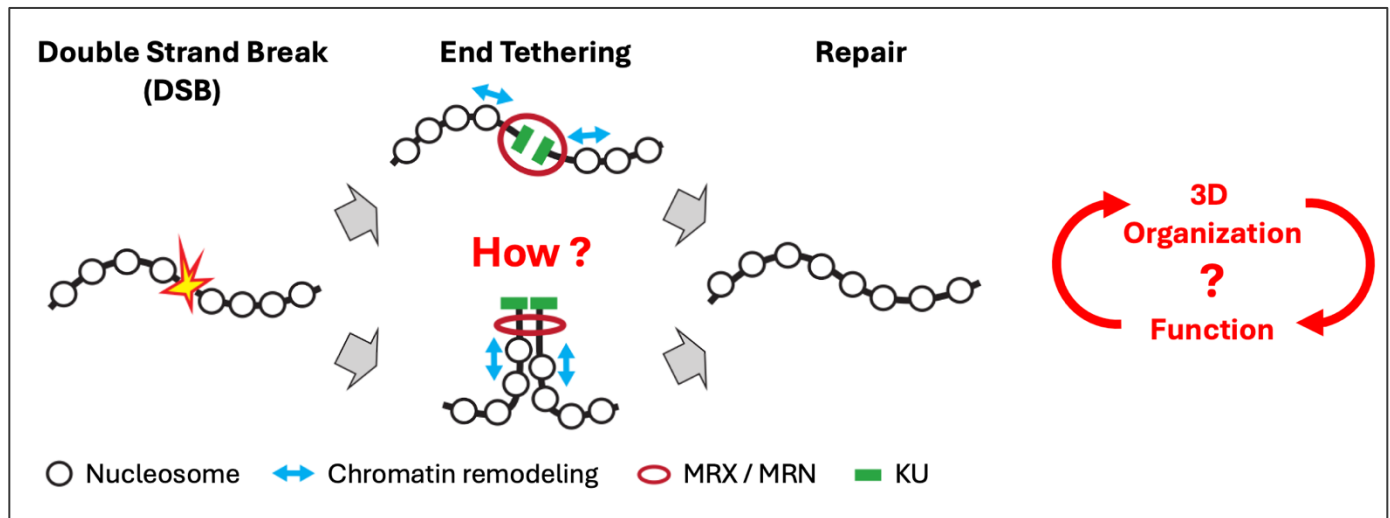




Understanding the role of chromatin architecture in the DNA Double Strand Break – DSB – Response

Date of the offer: Anytime from September 2026 to July 2027

Tuteur du stage et Laboratoire d'accueil / Internship supervisor and Host laboratory:

Laboratoire / Lab : Laboratoire de Biologie et Modélisation de la Cellule (LBMC)

Chef d'équipe / Team leader (name, function, e-mail and telephone): Axel Delamarre, Chercheur INSERM, axel.delamarre@ens-lyon.fr, 04 72 72 80 52

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Site internet de l'équipe / Team Website : <https://www.ens-lyon.fr/LBMC/equipes/carr>

Langues parlées dans l'équipe / Languages spoken in the lab: French, English



Titre du projet de recherche / Research project title:

Understanding the role of chromatin architecture in the DNA Double Strand Break – DSB – Response

Mots clés / Keywords : 3D genome organization • Double Strand Break (DSB) • Single-molecule methods • Chromatin • SMC complexes • Budding yeast

Techniques: Nanopore sequencing • Next Generation Sequencing (NGS) • Yeast genetics • PCP • CAD-C • Auxin-inducible degron AID • DSB) • Data analysis with bash and python and custom bioinformatics scripts

Description du projet / Project description (subject and technics):

Genotoxic stress responses are critical for maintaining genome stability after DNA double-strand breaks (DSBs). While this response is generally well characterized, key aspects remain unclear, particularly the 3D organization of chromatin around DNA lesions. Existing techniques like Hi-C and Micro-C lack the resolution needed for detailed analysis. Additionally, stress responses are multistep processes with unique dynamics, but high cell-to-cell variability complicates accurate interpretation. Traditional assays like ChIP-seq, MNase-seq, and Hi-C provide population-averaged data that conceals cell-to-cell heterogeneity and hinders accurate interpretation.

To address these issues, this project will use recently developed cutting-edge technologies like PCP and CAD-C. These methods detect multi-way chromatin interactions, DNA-bound protein footprints at base-pair resolution, and nucleosome spacing on single DNA molecules, offering unprecedented insights into chromatin structure and variability at the molecular level.

In the context of DSBs, the high resolution of PCP / CAD-C allows for examining End-Tethering mechanisms at a subnucleosomal scale. End-tethering appears to be independently regulated by the KU and MRX complexes in a competitive manner, influenced by chromatin remodeling at the break site. By analyzing interactions between KU, MRX, and chromatin remodelers, this project aims to identify DSB end-tethering's molecular mechanisms.

Additionally, the coordination between chromatin remodeling and end resection at DSBs remains poorly understood. Current models suggest that chromatin remodelers slide or remove nucleosomes as nucleases resect the 5' strand of DNA, but population-based methods average signals from millions of molecules, masking the co-occurrence of remodeling and resection. PCP will allow us to study this coupling at the single-molecule level, offering insights into the dynamic relationship between chromatin remodeling and end resection.

Overall, this project uses advanced methods to challenge established models and propose new ones, thereby advancing our understanding of 3D chromatin organization in response to DNA double-strand breaks.

This ambitious project is intended to be pursued in a PhD. You will work directly with the group leader on this project. Please contact Axel Delamarre if you are interested or need further information.

Publications du laboratoire ou revue recommandée sur le sujet / Lab publications or recommended review on the subject (5 max):

Delamarre A*, Reveil M, Pinto Pinchon D, Mohibullah N, Boemo M, Whitehouse I*. CAD-C reveals the near-perfect alignment of sister chromatids. Biorxiv 2025.
<https://www.biorxiv.org/content/10.64898/2025.12.18.694906v1>

Delamarre A, Bailey B, Yavid J, Koche R, Mohibullah N, Whitehouse I. Chromatin architecture mapping by multiplex proximity tagging. Molecular Cell. 2025.
[https://www.cell.com/molecular-cell/fulltext/S1097-2765\(25\)00547-7](https://www.cell.com/molecular-cell/fulltext/S1097-2765(25)00547-7)

Piazza A, Bordelet H, Dumont A, Thierry A, Savocco J, Girard F, Koszul R. Cohesin regulates homology search during recombinational DNA repair. Nature cell biology. 2021 Nov;23(11):1176-86.
<https://www.nature.com/articles/s41556-021-00783-x>

Phipps J, Toulouze M, Ducrot C, Costa R, Brocas C, Dubrana K. Cohesin complex oligomerization maintains end-tethering at DNA double-strand breaks. Nature cell biology. 2025 Jan;27(1):118-29.
<https://www.nature.com/articles/s41556-024-01552-2>