# Master 2 Reproduction et Développement
**Stage de recherche 2025-2026**

**Prénom et NOM de l'encadrant : Aurore SANCHEZ**

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**Intitulé de l 'équipe d'accueil :** Chromosome Dynamics and Recombination

**Site internet de l'unité :** https://curie.fr/unite/umr3244 , https://institut-curie.org/team/borde

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**Résumé du thème de recherche de l'équipe d'accueil (une dizaine de lignes maximum) :**

The Chromosome Dynamics and Recombination team led by Valérie BORDE, investigates **homologous recombination** and its essential role in maintaining genome stability and ensuring accurate chromosome segregation during the formation of haploid gametes in meiosis. We use a combination of **genetic, genomic, proteomic, and molecular biology** approaches, with the yeast *Saccharomyces cerevisiae* as our model organism.

The team is based at the Institute Curie, one of the leading cancer research centers. The Institute provides access to state-of-the-art technological platforms, such as High-Throughput Sequencing and Proteomics facilities, which will be essential for this project.

Aurore SANCHEZ, a CNRS researcher, is seeking a Master 2 student in biology to join the Borde group. The team currently includes one Principal Investigator (PI), one CNRS researcher, two engineers, two assistant engineers, a postdoctoral researcher, and two PhD students, for a total of nine members. https://institut-curie.org/team/borde

**Titre du projet de stage :**

**Projet de stage : (une vingtaine de lignes maximum)**

**Research subject**

Homologous recombination occurs when a chromosome carrying a double-stranded DNA break (DSB) uses a homologous sequence as a template for repair. This leads to the exchange of genetic material between parental chromosomes through **crossing-over**, a fundamental source of genetic diversity. Defects in this process can have severe clinical consequences, being linked to hereditary cancers, genomic instability syndromes, and infertility in mammals. Despite decades of study, many molecular details of meiotic recombination remain elusive, partly because:

1. Many factors involved in DSB repair are still unknown.
2. Known factors act at distinct and tightly regulated stages of homologous recombination, complicating their detection and functional analysis.

Recently, our team has developed an innovative experimental system that allows us to separate the

early and late stages of homologous recombination. Coupled with cutting-edge technologies already established or under development in the lab, this system provides a unique opportunity to identify and characterize new, stage-specific factors involved in meiotic recombination.

**Missions**

The candidate will contribute to uncovering and characterizing the molecular players involved in crossing-over formation, using our system that allows the temporal separation of early and late recombination steps.
The **M2 internship** will have two main objectives:

1. **Identify novel recombination factors** involved in the later steps of homologous recombination through proteomic screening approaches (using methods derived from BioID).
2. **Characterize both newly identified factors (from Task 1) and previously suspected factors** by:
    - Validating their presence at recombination sites via chromatin immunoprecipitation (ChIP).
    - Analyzing the consequences of their inactivation *in vivo* (e.g., effects on gamete viability, recombination efficiency, distribution, and nature of recombination events).

The candidate will use techniques routinely employed in the lab and help implement a global proteomic strategy to discover and investigate the roles of these factors in the final stages of homologous recombination.

**Techniques mises en œuvre par le stagiaire :**

The techniques will therefore involve molecular biology, ChIP qPCR, proteomics and genetics. Our model organism is the budding yeast, which allows to finely decipher the molecular mechanisms at play, and shows a high conservation with mammalian cells in terms of homologous recombination

**Publications du Responsable de stage au cours des 5 dernières années** :

1. Roy, M*., **Sanchez, A*#**., Guerois, R., Senoussi, I., Cerana, A., Sgrignani, J., Cavalli, A., Rinaldi, A., et Cejka, P#., **2025.** EXO1 Promotes the Meiotic MLH1-MLH3 Endonuclease through Conserved Interactions with MLH1, MSH4 and DNA. **Nature Communications** 16, no 1 (3 mai 2025): 4141. https://doi.org/10.1038/s41467-025-59470-2. ***Equal contribution, # Co-Corresponding authors**

2. Ceppi, I., Dello Stritto, MR., Mütze, M., Braunshier, S., Mengoli, V., Reginato, G., Phúc Võ, HM., Jimeno, S., Acharya, A., Roy, M., **Sanchez, A**., Halder, S., Howard, SM., Guérois, R., Huertas, P., and Cejka, P., **2025**. *Mechanism of BRCA1-BARD1 function in DNA end resection and DNA protection* **Nature**. http://dx.doi.org/10.1038/s41586-024-07909-9

3. Legrand, S., Saifudeen, A., Bordelet, H., Vernerey, J., Guille A., Bignaud, A., Thierry, A., Acquaviva, L., Gaudin, M., **Sanchez, A**., Johnson, D., Friedrich, A., Schacherer, J., Neale, MJ., Borde, V.,Koszul, R., Llorente, B., **2024.** *Absence of chromosome axis protein recruitment prevents meiotic recombination chromosome-wide in the budding yeast Lachancea kluyveri*. **Proc. Natl. Acad. Sci**. U. S. A. 121, e2312820121 https://doi.org/10.1073/pnas.2312820121

4. Mengoli, V., Ceppi, I., **Sanchez, A**., Cannavo, E., Halder, S., Scaglione, S., Gaillard, PH., McHugh, P., Riesen, N., Pettazzoni, P., Cejka, P., **2022**. *WRN helicase and mismatch repair complexes independently and synergistically disrupt cruciform DNA structures.* **The EMBO Journal** https://doi.org/10.15252/embj.2022111998

5. Halder, S., **Sanchez,** A., Ranjha, L., Reginato, G., Ceppi, I., Acharya, A., Anand, R., Cejka, P., **2022**. *Double-stranded DNA binding function of RAD51 in DNA protection and its regulation by BRCA2*. **Mol Cell** https://doi.org/10.1016/j.molcel.2022.08.014

6. Dai*****, J., **Sanchez*, A**., Adam, C., Ranjha, L., Reginato, G., Chervy, P., Tellier-Lebegue, C., Andreani, J., Guérois, R., Ropars, V., Du, M.-H.L., Maloisel, L., Martini, E., Legrand, P., Thureau, A., Cejka, P., Borde, V., Charbonnier, J.-B., **2021**. *Molecular basis of the dual role of the Mlh1-Mlh3 endonuclease in MMR and in meiotic crossover formation***. Proc. Natl. Acad. Sci**. 118.
https://doi.org/10.1073/pnas.2022704118 ***Equal contribution**

7. Cannavo*****, E., **Sanchez*, A**., Anand*****, R., Ranjha, L., Hugener, J., Adam, C., Acharya, A., Weyland, N., Aran-Guiu, X., Charbonnier, J.-B., Hoffmann, E.R., Borde, V., Matos, J., Cejka, P., **2020**. *Regulation of the MLH1–MLH3 endonuclease in meiosis*. **Nature** 586, 618–622. https://doi.org/10.1038/s41586-020-2592-2 ***Equal contribution**

8. Bennett, L.G., Wilkie, A.M., Antonopoulou, E., Ceppi, I., **Sanchez, A**., Vernon, E.G., Gamble, A., Myers, K.N., Collis, S.J., Cejka, P., Staples, C.J., **2020**. *MRNIP is a replication fork protection factor.* **Sci. Adv**. 6, eaba5974. https://doi.org/10.1126/sciadv.aba5974

9. **Sanchez, A**., Adam, C., Rauh, F., Duroc, Y., Ranjha, L., Lombard, B., Mu, X., Wintrebert, M., Loew, D., Guarné, A., Gnan, S., Chen, C.-L., Keeney, S., Cejka, P., Guérois, R., Klein, F., Charbonnier, J.-B., Borde, V., **2020**. *Exo1 recruits Cdc5 polo kinase to MutLy to ensure efficient meiotic crossover formation*. **Proc. Natl. Acad. Sci**. 117, 30577–30588. https://doi.org/10.1073/pnas.2013012117

**Autres informations:**

**Etudiants actuellement en thèse ou en M2 dans l'équipe d'accueil.** Pour chaque étudiant indiquez le nom du responsable de thèse, l'année du début de la thèse et l'Ecole Doctorale de rattachement

- Emilie Mylne – resp. Valérie Borde – thèse depuis octobre 2021 – ED CDV
- Andreu Pujolar Ramos- resp. Valérie Borde – thèse depuis novembre 2024 – ED SDV PSL

**Etudiants ayant préparé ou soutenu leur thèse ou leur M2 dans l'équipe d'accueil au cours des six dernières années.** Pour chaque étudiant indiquez le nom du responsable de l'étudiant, l'année du début de la thèse et de fin de la thèse, l'Ecole Doctorale de rattachement et le devenir de l'étudiant.

Alexandra Pyatnitskaya – resp. Arnaud De Muyt/Valérie Borde – thèse octobre 2017- soutenue octobre 2021– ED CDV – postdoctorat à Aberdeen, Ecosse (équipe Anne Donaldson)

**Cette proposition de stage s'adresse-t-elle spécifiquement à un étudiant scientifique, médecin ou vétérinaire ou bien est-il ouvert à tous les profils ?**

Étudiant scientifique

**Ce sujet peut-il donner lieu à une thèse ?**

OUI.

Ecole doctorale: SDV PSL