EuReCa International PhD Program

PhD thesis project

2022 Call for application

Impact of transposable element activity on genome stability and organization during meiosis

General information

Call	2022
Reference	2022-03-BOURCHIS
Keyword(s)	Transposable elements; Meiosis; Chromatin; DNA methylation; Genome stability; Nuclear organization

Director(s) and team

Thesis director(s)	Deborah Bourc'his
Research team	Epigenetics decisions and Reproduction
Research department	U934/UMR 3215 Genetics and Developmental Biology

Description of the PhD thesis project

Transposable elements (TEs) are mobile genetic entities that are present by millions in mammalian genomes. Their effects are pleiotropic, from insertional mutagenesis to chromatin position effects or chromosome rearrangements. While TEs have prompted useful innovations during evolution, they constitute a genomic threat in the short term. Accordingly, cells use several strategies to tam TEs, among which DNA methylation plays a key role. Importantly, TE activity has been linked to several diseases, including cancer and infertility. Notably, our team previously showed that meiosis is particularly vulnerable to TE activity: when TEs fail to be repressed during male germline development, homologous chromosome pairing is impaired at meiosis, leading to spermatogenesis interruption and male sterility.

The project aims at deciphering the relationship between TEs and meiosis, using two unique mouse models of TE reactivation, resulting from deficient DNA methylation or from temporally controlled CRISPR-based activation. Innovative genomic, bioinformatic and microscopy approaches will be carried out to:

1) investigate the impact of TE activity on the meiotic chromatin landscape and distribution of recombination sites,
2) investigate the impact of TE activity on meiotic chromosome conformation
3) control in space and time TE reactivation during meiosis.

We hope to uncover how TEs influence chromosome integrity, with broad implications for reproductive and cancer research.

International, interdisciplinary & intersectoral aspects of the project

This is an interdisciplinary project, at the interface between molecular and cell biology, and bioinformatic/biostatistic analyses specifically adapted to the study of repeated transposable elements. The student will have the opportunity to interact with international experts in the corresponding fields. In particular, we benefit from the support of Andres Canela (NIH and Kyoto University), who recently developed a technique that allows quantitatively capturing single stranded DNA. Finally, stimulated emission depletion (STED) super-resolution microcopy will be refined for our purpose with ABBERIOR (provider of the STEDYCON), with the help of the BDD Imaging Platform of the Institut Curie.

Recent publications

1. Chelmicki T., Roger E., Teissandier A., Dura M., Bonneville L., Rucli S., Dossin F., Fouassier C., Lameiras S. and **Bourc'his D**. (2021). m6A RNA methylation regulates the fate of endogenous retroviruses. Nature 591, 312-316. doi: 10.1038/s41586-020-03135-1

2. Dura M., Teissandier A., Armand M., Barau J., Bonneville L., Weber M., Baudrin L.G., Lameiras S. and **Bourc'his D**. DNMT3A-dependent DNA methylation is required for spermatogonial stem cells to commit to spermatogenesis. (2021). bioRxiv, doi: https://doi.org/10.1101/2021.04.19.440465

3. Molaro A., Malik H.S and **Bourc'his D**. (2020). Dynamic evolution of de novo DNA methyltransferases in rodent and primate genomes. Mol Biol Evol 37, 1882-1892. doi: 10.1093/molbev/msaa044

4. Teissandier A., Servant N., Barillot E. and **Bourc'his D**. (2019). Tools and best practices for retrotransposon analysis using high-throughput sequencing data. Mobile DNA 10, 52. doi: 10.1186/s13100-019-0192-1

5. Barau J., Teissandier A., Zamudio N., Roy S., Nalesso V., Hérault Y., Guillou F. and **Bourc'his D**. (2016). The DNA methyltransferase DNMT3C protects male germ cells from transposon activity. Science 354, 909-912. doi: 10.1126/science.aah5143

Expected profile of the candidate

We are looking for a PhD candidate with strong motivation for basic research, and potential for independent and creative thinking. Applicants should show proof of their ability to work in different lab environments and their potential for adapting to different research topics and/or techniques (geographical and thematic/technical mobility). Background in mouse genetics and/or chromatin biology is recommended. Previous knowledge in mammalian reproduction or meiosis would be a plus, but not compulsory.