PhD Thesis Project (M/F)

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

The hosting structure

The Curie Institute Research Center
The Institut Curie is a major player in the research and fight against cancer. It consists of a hospital and a Research Center of more than 1000 employees with a strong international representativeness.
The objective of the Curie Institute Research Center is to develop basic research and to use the knowledge produced to improve the diagnosis, prognosis, and therapeutics of cancers as part of the continuum between basic research and innovation serving the patient.

Context

Laboratory

- 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.

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

International, interdisciplinary & intersectoral aspects of the project

- **International:** 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.
- **Interdisciplinary:** 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.
- **Intersectoral:** 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.

Candidate Profile

- 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

All our opportunities are open to people with disabilities

Contract information

Type of contract: Fixed-term contract
Starting date: September 1st, 2022
Duration: 3 *y*ears
Working time: full time
Remuneration: 2.123 € gross / month
Benefits*:* Collective catering, reimbursement of transportation fees up to 70%, supplementary health insurance
Location of the position: Paris

Contact

Application process

Only via the online application (https://training.institut-curie.org/eureca). **Email applications are not accepted**.

To know more about the eligibility criteria and the online application process, please check the website https://training.institut-curie.org/eureca or contact phd.eureca@curie.fr

Publication date: 20/12/2021
Deadline for application: 10/01/2022.

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