PhD position

**Specificities of homologous recombination during meiosis: importance of the MEIOB-SPATA22 complex**

in the Laboratory of the development of the Gonads, headed by Pr. Gabriel Livera, IRCM, CEA of Fontenay aux roses (92265), south of Paris

supervision Dr. Emmanuelle Martini Emmanuelle.martini@cea.fr

 Homologous recombination (HR) is a widely conserved genetic mechanism essential for genome integrity. Mutations and deregulated expression of HR genes are associated with tumorigenesis and infertility. In somatic cells, HR is a DNA repair pathway that mainly occurs between sister chromatids to minimize genomic rearrangements and maintain genome integrity. During meiosis in germ cells, HR repairs meiotic programmed double strand breaks to form a physical connection between homologous chromosomes (through crossover, CO) to generate diversity, properly segregate parental chromosomes and produce viable gametes. In the last decade, the meiosis-specific factors SPATA22, MEIOB, HSF2BP/MEILB2 were identified by our team and others. Their importance in meiosis was demonstrated thanks to engineered mouse models, but their exact roles are still poorly understood. Based on the observed phenotype of their corresponding mouse KO, these factors are thought to play crucial and interplaying roles during a key step of meiotic HR: the loading and dynamics of the recombinase RAD51 and its meiotic specific homolog DMC1.

**Project**

 Our team identified MEIOB and showed that it interacts with SPATA22, RPA and ssDNA to form a meiosis-specific complex. In the absence of MEIOB or SPATA22 HR is aborted preventing gamete formation. Recently, HSF2BP/MEILB2 was identified as a BRCA2 interactor essential for loading RAD51 and DMC1 during meiotic HR and has been shown to interact with MEIOB and SPATA22 in mouse testis. Depletion of HSF2BP leads to a drastic reduction in RAD51-DMC1 foci in spermatocytes, an accumulation of SPATA22 and finally male infertility. Published and preliminary results suggest that SPATA22 interacts directly with HSF2BP, suggesting that MEIOB-SPATA22 and HSF2BP could work together to ensure the formation, dynamic and activity of the recombinogenic filament formed by RAD51 and DMC1. The aim of this project is to combine in vivo and in vitro approaches using mutant mice, co-immunprecipitation, organ cultures and over-expression in human cells to better characterize how HSF2BP-BRME1, MEIOB-SPATA22 and BRCA2 interplay could influence the RAD51/DMC1 recombinogenic filament assembly and activity allowing proper meiotic HR and crossover formation and consequently gamete integrity. The achievement of this project will benefit from our team's strong expertise in germ cell differentiation and meiotic progression in mammals. This expertise is sustained by the discovery of multiple factors and the development of in vitro organ culture. This project is currently founded by the ANR, MEIOSPHR.

**Key words:**

meiotic recombination, DNA repair, fertility, cancer

**Location:**

Our lab, headed by Pr. Gabriel Livera, is located at the CEA of Fontenay aux roses in the south suburb of PARIS in the unit "Stabilité Génétique, Cellules souches et radiations" in the institute Francois Jacob

Our lab is composed of 3 teachers-researchers, 2 researchers and 3 assistant engineers

The candidate will benefit of the in-house platforms such as animal facility, microscopy, cloning and protein purification, cell sorting.

**Candidate profile:**

-master in biology with knowledge in genetic, molecular and cellular biology

- interest in genome stability and DNA repair process

- strong motivation and interest for the project

- English B2 level will be appreciated

**Contract:**

- fixed term contract of 3 years founded by the CEA + a possibility of 1 year extension

- student school: ED BioSPC université Paris Cité

**Contact**

To apply or obtain more information please contact directly Emmanuelle Martini by email: Emmanuelle.martini@cea.fr

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