Stage proposé par

Nom et adresse du Laboratoire ou de l'Unité : Unité Stabilité Génétique, Cellules Souches et Radiations,
Laboratoire de Développement des gonades
18 route du panorama, 92265 Fontenay-Aux-Roses

Téléphone : 01 46 54 80 04
Mail :Emmanuelle.martini@cea.fr
Site internet : https://jacob.cea.fr/drf/ifrancoisjacob/Pages/Departements/IRCM/Equipes/LDG.aspx
Directeur du Laboratoire ou de l'Unité : Pr Gabriel LIVERA (Laboratoire), Dr François BOUSSIN (Unité)

Intitulé de l 'équipe d'accueil : Laboratoire de Développement des gonades (Equipe Recombinaison homologue méiotique)

Prénom et NOM du Responsable de l'équipe : Gabriel LIVERA (Laboratoire), Emmanuelle Martini (Equipe)

Résumé du thème de recherche de l'équipe (une dizaine de lignes maximum)
Notre laboratoire, le LDG s'intéresse aux mécanismes fondamentaux contrôlant le développement des cellules germinales fœtales murines et humaines et à leur altération par les perturbateurs endocriniens et les rayonnements ionisants.
L'équipe Recombinaison homologue méiotique s'intéresse aux acteurs impliqués dans la recombinaison homologue et à leurs partenaires.

Titre du projet de stage : Role of RAD50 Protein in Meiotic Chromosome Integrity

Prénom, NOM, téléphone et adresse e-mail du Responsable du stage: Emmanuelle Martini, Emmanuelle.martini@cea.fr

Projet de stage : (une vingtaine de lignes maximum)

DNA Double-strand breaks (DSBs) can be accidental or programmed, and if not repaired, they can lead to chromosomal translocations, aneuploidy, and cancer risks. Homologous recombination (HR) is one of the main pathways to repair these breaks. HR is essential to maintain genome integrity and generates genetic diversity during meiotic division in germ cells. The MRN complex, composed of MRE11, RAD50, and NBS1, is crucial in the detection, signaling, and repair of DSBs through HR. It also important to preserve telomere integrity by stabilizing their structure and facilitating their extension. We know that RAD50 is important in the formation and resection of DSBs during meiosis, but other roles, such as telomere dynamics and checkpoint activation during this stage, remain to be explored. This project aims to characterize a new mouse mutant model of RAD50 to study these roles independently of resection. The mutant mouse is sterile, and our preliminary data indicate that meiotic cells are arrested with persistent meiotic breaks. The aim of this study is to understand what blocks meiotic progression in the *Rad50* mutant mice through in vivo and in vitro approaches, using immunolocalizations of specific factors on meiotic cells and extracts. We will search for meiotic partners of the MRN complex through co-immunoprecipitation of the complex and its partners, followed by mass spectrometry analysis, and determine if these partners can be affected by the mutation. This will be followed by a physical and functional analysis of these interactions. With this new mutant, we aim to identify new functions of RAD50 and the MRN complex in genome integrity. This work can be followed by a PhD.

Techniques mises en œuvre par le stagiaire :
-Immunofluorescence

-WesternBlot
-Etalement de chromosomes.

Publications du Responsable de stage au cours des 5 dernières années :
- In vivo reduction of RAD51-mediated homologous recombination triggers aging but impairs oncogenesis. Matos-Rodrigues, G et al. EMBO.2023
- Foetal exposure to the bisphenols BADGE and BPAF impairs meiosis through DNA oxidation in mouse ovaries. Abdallah, S . Env Poll. 2022
- Mouse model of radiation-induced premature ovarian insufficiency reveals compromised oocyte quality: implications for fertility preservation. Puy, V et al. Biomed Repro. 2021
- Molecular basis of the dual role of the Mlh1-Mlh3 endonuclease in MMR and in meiotic crossover formation. Dai JQ et al.PNAS.2021
- Mouse Models for Deciphering the Impact of Homologous Recombination on Tumorigenesis. Matos-Rodrigues, G et al .CANCERS.2021
- The meiosis-specific MEIOB-SPATA22 complex cooperates with RPA to form a compacted mixed MEIOB/SPATA22/RPA/ssDNA complex. Ribeiro et al. DNA repair. 2021
- shani mutation in mouse affects splicing of Spata22 and leads to impaired meiotic recombination. Petrillo et al. Chromosoma. 2020

Autres informations:

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