Master 2 Reproduction et Développement
Stage de recherche 2026-2027

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Intitulé de l 'équipe d'accueil : Laboratoire du Développement des Gonades

Site internet de l'unité : Laboratoire de Développement des Gonades

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

My research group investigates how DNA damage response and repair mechanisms shape the biology of germ cells, with applications spanning both **cancer vulnerability** and **fertility preservation**. This group is part of the LDG (headed by G. Livera) that studies normal and altered mammalian gametogenesis, with a special emphasis on the molecular events essential to produce healthy and functional gametes. The strength of the LDG is the strong interconnection existing between 4 axes: Repro-toxicology, Meiosis initiation, DNA repair & meiotic recombination, Metabolism & Germ cell differentiation.

I propose to the student to choose between two projects:

In one project, we study a mutation in a DNA repair complex (MRN) that makes mouse germ cells infertile without harming other tissues—since cancer cells share similar traits (fast growth, telomere maintenance), we're testing whether this vulnerability could be used to selectively kill tumor cells. In a second project, we're investigating why immature egg cells are extremely sensitive to radiation, by studying how they choose between different DNA repair pathways—work that could help protect fertility in young cancer patients.

Titre du projet de stage :

projet #1

From Mechanism to Fertility Preservation: Targeting DNA Repair Pathways to Protect the Ovarian Reserve"

projet #2

From Fertility to Malignancy: Shared MRN-Dependent Vulnerabilities in Germ Cells and Cancer

Projet de stage : (une vingtaine de lignes maximum)

Projet #1

Preserving ovarian function during oncological treatment is an increasing clinical priority, yet ovarian toxicity remains poorly understood due to limited mechanistic insight and standardized models. Chemotherapy and radiotherapy are well-established, dose-dependent causes of gonadotoxicity and premature ovarian insufficiency (POI). Our lab showed that 0.3 Gy fully depletes primordial follicles in mice, while growing follicles survive 2 Gy. We hypothesized this reflects a shift in DNA repair pathway usage during folliculogenesis: primordial follicles rely exclusively on homologous

recombination (HR), while growing follicles engage both HR and non-homologous end joining (NHEJ) after IR. This HR-to-NHEJ shift may underlie their differential radiosensitivity, though its regulation remains unexplored. Building on this, we established an in vitro culture model of prepubertal ovarian fragments to dissect this mechanism using pathway-specific inhibitors, circumventing lethality issues seen in knockout models

Projet #2

This project exploits shared biological features between germ cells and cancer cells to identify tumor-specific vulnerabilities. Germ cells rapidly expand, migrate, and maintain telomeres—properties resembling cancer cells—suggesting that mechanisms essential for germ cell integrity may be exploitable weaknesses in cancer. We focus on the MRE11–RAD50–NBS1 (MRN) complex, a conserved DNA damage response factor involved in double-strand break repair, checkpoint activation, and telomere maintenance, whose dysregulation is linked to cancer predisposition and therapy resistance. Using a mouse knock-in model of a patient-derived RAD50 mutation (E1035Δ), we found homozygous mutants are healthy but sterile, with reduced proliferating germ cells and meiotic arrest—a separation-of-function mutation affecting MRN specifically in germ cells, with associated telomere defects. We hypothesize this vulnerability extends to cancer cells sharing similar properties, and will define the molecular defect and assess effects on cancer cell proliferation in vivo and in vitr

Techniques mises en œuvre par le stagiaire :

molecular, Cellular and genetic approaches :

Immunolocalization, organ and cell cultures, histology, protein extract, co-immunprecipitations, western blot, drug treatment with genotoxic agents

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

Bellutti L, Chan Sock Peng E, Cluzet V, Guerquin M-J, Rolland A, Messiaen S, Llano E, Dereli I, **Martini E**, Tóth A, Pendás AM, Chalmel F*, Livera G* (2025) Genome-wide transcriptional silencing and mRNA stabilization allow the coordinated expression of the meiotic program in mice. *Nucleic Acids Res*, **53:** gkaf146

Matos-Rodrigues G, Barroca V, Muhammad AA, Dardillac E, Allouch A, Koundrioukoff S, Lewandowski D, Despras E, Guirouilh-Barbat J, Frappart L, Kannouche P, Dupaigne P, Le Cam E, Perfettini JL, Romeo PH, Debatisse M, Jasin M, Livera G, **Martini E***, Lopez BS* (2023) In vivo reduction of RAD51-mediated homologous recombination triggers aging but impairs oncogenesis. *EMBO J*, e110844

Matos-Rodrigues G, Guirouilh-Barbat J, **Martini E**, Lopez BS* (2021a) Homologous recombination, cancer and the 'RAD51 paradox'. *NAR Cancer*, **3:** zcab016

Matos-Rodrigues G, **Martini E*,** Lopez BS (2021b) Mouse Models for Deciphering the Impact of Homologous Recombination on Tumorigenesis. *Cancers (Basel)*, **13:**

Petrillo C, Barroca V, Ribeiro J, Lailler N, Livera G, Keeney S, **Martini E*,** Jain D* (2020) shani mutation in mouse affects splicing of Spata22 and leads to impaired meiotic recombination. *Chromosoma*, **129:** 161–179

Ribeiro J, Dupaigne P, Petrillo C, Ducrot C, Duquenne C, Veaute X, Saintomé C, Busso D, Guerois R, **Martini E*,** Livera G (2021) The meiosis-specific MEIOB-SPATA22 complex cooperates with RPA to form a compacted mixed MEIOB/SPATA22/RPA/ssDNA complex. *DNA Repair (Amst)*, **102:** 103097

*** corresponding author**

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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

Hajar SAIDI, Emmanuelle MARTINI, BIOSPC 2024-

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.

Hajar SAIDI thèse Emmanuelle MARTINI, BIOSPC 2024-
Cathy SAAB M2 + These, Emmanuelle MARTINI BIOSPC 2020-2024 *Post Doc Institut Gustave Roussy*
Gabriel De MATOS RODRIGUES thèse, Emmanuelle MARTINI co-direction ED 582 2018-2020 Paris Saclay, *CR CNRS Institut Gustave Roussy*.
Yasmine LAKERMI M2, Emmanuelle MARTINI 2023

Michelle NASR, thèse Marie-Justine GUERQUIN BIOSPC 2025-
Amandine JAMPY M2, + thèse Marie-Justine GUERQUIN BIOSPC 2019-2024 *Enseignante prepa*
Antoine Gillet M2, Marie-Justine GUERQUIN 2020-2021
Lionnel MONGIS M2, Marie-Justine GUERQUIN 2020-2021

Anna CLOAREC these, Gabriel LIVERA BIOSPC 2024-
Morgane LEBEUZE these, Gabriel LIVERA 2023-
Pauline MOISON these, Gabriel LIVERA BIOSPC 2020-2023 *coordinatrice projets APHP*
Vincent PUY thèse, Gabriel LIVERA ED 568 Paris Saclay 2017-2021 MD APHP
Lea OLIVERA M2, Gabriel LIVERA 2023-24
Leatitia RANAIVOHA M2, Gabriel LIVERA 2021-22
Clara PHAN M2, Gabriel LIVERA 2022-23

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 ?
ouvert à tous profils

Ce sujet peut-il donner lieu à une thèse ?
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