Master 2 Reproduction et Développement
Stage de recherche 2024-2025

Stage proposé par

Nom et adresse du Laboratoire ou de l'Unité :
Institut de Génétique, Reproduction et Développement
CNRS UMR6293, INSERM U.1103, Université Clermont Auvergne,
28 Place Henri Dunant, Clermont-Ferrand, France.

Téléphone : 0473178177
Mail : antoine.molaro@uca.fr
Site internet : https://www.igred.fr/en/team/evolutionary-epigenomics-and-genetic-conflicts/
Directeur du Laboratoire ou de l'Unité : Krzysztof Jagla

Intitulé de l 'équipe d'accueil : Evolutionary Epigenomics and Genetic Conflicts

Prénom et NOM du Responsable de l'équipe : Antoine MOLARO

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

Our team studies the evolution of germline chromatin pathways and the epigenome. More specifically, we focus on understanding how past and ongoing genetic conflicts shaped the function of the epigenome. We combine phylogenetic approaches with *in vivo* epigenome profiling to identify genetic innovations in chromatin pathways and characterize their function (*e.g.*, see Molaro *et al.*, *Genome Research*, 2018; *Mol. Biol. Evol.*, 2020, Mordier et al., *BioRxiv* 2024). We study these questions in normal and pathological contexts, using mouse models and mammalian tissue culture (*e.g.,* see Molaro *et al.*, *PLoS Biology*, 2020; Chew *et al.*, *Nature Comm.*, 2021; Karam & Molaro, *Chromosoma* 2023). Our lab is located at the Institute of Genetics, Reproduction and Development (iGReD). Our team started in 2020 and we are currently supported by the FRM, ANR and the INSERM.

Titre du projet de stage : Consequences of Short Histone H2A Rapid Evolution on Chromatin Organization

Prénom, NOM, téléphone et adresse e-mail du Responsable du stage: Antoine MOLARO

Projet de stage : (une vingtaine de lignes maximum)

Background: Histones are evolutionary conserved proteins that package genetic information into nucleosomes - the basic unit of chromatin. In placental mammals, including in humans, a unique class of short H2A histone variants are incorporated in the chromatin of reproductive cells. The loss of short H2As in mouse models affects fertility and development. In addition, their ectopic activation in cancer cells leads to chromatin reorganization. Unlike other histones, short H2As are subject to dramatic evolutionary innovations. Although these innovations occur over protein domains predicted to impact histone function, their functional consequences on chromatin structure have never been explored *in vivo* .

Project: This Master project is aimed at identifying and comparing the chromatin features of cells expressing specific short H2A orthologs. This will help understand their role during reproduction and cancer. Using phylogenetics we will identify and clone human and non-human primate short H2As sequences for expression in cell culture. Using microscopy, qPCR and high-resolution chromatin profiling we will compare the chromatin alterations induced by specific short H2A orthologs. During her/his time in the lab, the student will develop skills in: evolution-guided hypothesis testing, molecular and cell biology, epigenomics and bioinformatics. The student will work in a diverse and inclusive

environment. This project uniquely combines evolutionary and chromatin biology and is well-suited for students seeking to pursue a career in laboratory research or a doctorate in biological sciences.

Requirements: good command of research literature; prior experience with laboratory techniques and protocols (e.g. internship…); comfortable with note-keeping and oral presentations.

Techniques mises en œuvre par le stagiaire :

- Phylogenetics
- Vector design and building
- Transfections in mammalian cell lines
- Microscopy
- qPCR
- CUT&RUN or CUT&TAG

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

Selected publications related to the internship. $ corresponding author

Mordier J, Fraisse M, Cohen-Tannoudji M, **Molaro A**$. Recurrent evolutionary innovations in rodent and primate Schlafen genes. **2024** bioRxiv https://doi.org/10.1101/2024.01.12.575368

Karam G, **Molaro A**$. Casting histone variants during mammalian reproduction. *Chromosoma*, **2023** Sep;132(3):153-165. PMID: 37347315

Raman P, Rominger C, Young JM, **Molaro A**, Tsukiyama T, Malik HS. Novel classes and evolutionary turnover of histone H2B variants in the mammalian germline. *Molecular Biology and Evolution.* **2022.** 3;39(2):msac019. PMID: 35099534

Chew GL, Bleakley M, Bradley R, Henikoff S, Malik HS, **Molaro A**$ & Sarthy J$. Short H2A Histone Variants are Expressed in Cancers. *Nature Communications*. **2021***. vol. 12 (1) , pp. 490, 2021.* PMID: 33473122

Molaro A$, Wood AJ, Janssens D, Kindelay SM, Eickbush MT, Wu S, Singh P, Muller CH, Henikoff S and Malik HS$. Biparental contributions of the H2A.B histone variant control embryonic development in mice. *PLoS Biology. **2020**. vol. 18 (12) , pp. e3001001.* PMID: 33362208

Molaro A$, Malik HS, Bourc'his D$. Dynamic evolution of de novo DNA methyltransferases in rodent and primate genomes. *Molecular Biology and Evolution.* **2020***; 37(7):1882-1892.* PMID: 32077945

Molaro A, Young JA, Malik HS. Evolutionary origins and diversification of testis-specific short histone H2A variants in mammals. *Genome Research*. **2018**; 28(4): 460-473. PMID: 29549088

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

- 2024 Naell Lenoir, ED 65, SVSAE, responsable de thèse Antoine Molaro
- 2022 Germaine Karam, ED 65, SVSAE, responsable de thèse Antoine Molaro

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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.

- 2020-2021 Guillaume Buisson, Université Clermont Auvergne ; responsable Antoine Molaro

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 ?

Étudiant en science de la vie

Ce sujet peut-il donner lieu à une thèse ?

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