

**Track « Integrative Biology, Physiopathologies »**  
**Proposal for a Master 2 internship – 2024-2025**

**Title :** Consequences of Short Histone H2A Rapid Evolution on Chromatin Organization

**Laboratory :** Institute of Genetics Reproduction and Development (iGReD); Team:  
“[Evolutionary Epigenomics and Genetic Conflicts](#)”

**Laboratory director :** Krzysztof Jagla

**Address :** Faculté de Médecine 28 Place Henri Dunant, 63000, Clermont-Ferrand.

**Internship tutor :** Antoine Molaro (Group Leader)

**Tel :** 0473178177

**e-mail :** antoine.molaro@uca.fr

**Summary :**

**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.

**Methodologies (key words) :** *phylogenetics; vector design and building; transfections in human and chimpanzee cell lines; microscopy; qPCR; CUT&RUN*

**Publications of the research group on the proposed topic (3 max.)**

1. Chew et al., 2021. Short H2A variants are expressed in cancer. *Nature Comm.* PMID: 33473122
2. Molaro A et al., 2020. Biparental contributions of the H2A.B histone variant control embryonic development in mice. *PLOS BIOLOGY.* PMID: 33362208
3. Molaro A et al., 2018. Evolutionary origins and diversification of testis-specific short histone H2A variants in mammals. *Genome Research.* PMID: 29549088