

## Track « Integrative Biology, Physiopathologies »

### Proposal for a Master 2 internship – 2023-2024

**Title :** Exploring the function of the unusual histone H2A.P during development

**Laboratory :** Genetic Reproduction and Development Institute (iGReD), Team: Evolutionary Epigenomics and Genetic Conflicts

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**Summary :** 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 deposited in the chromatin of reproductive cells. The loss of short H2As in mouse model leads to developmental defects, while their ectopic induction is associated with human cancer (see publications). Unlike other histones, short H2As are subject to dramatic evolutionary innovation. This diversification appears to result from of an ongoing genetic conflict between short H2A families, most notably between H2A.B and H2A.P. Yet, the *in vivo* functions of H2A.P remains unexplored to this day. Unlike many other short H2As, H2A.P is found in both human and mouse and its expression pattern suggests a function beyond reproductive cells.

**Project:** This master project is aimed at investigating the functional consequences of H2A.P loss and characterizing the chromatin landscapes of H2A.P containing nucleosomes. The student will take advantage of our in-house mouse models (KO and KI) to profile the chromatin and expression landscapes of H2A.P WT and KO germline cells. They will also help built inducible H2A.P cell lines to characterize the features of H2A.P nucleosomes in human and mouse. During her/his time in the lab, the student will develop skills in evolutionary, developmental and molecular biology. The student will work in a diverse and inclusive environment. This project is well-suited for students seeking to pursue careers 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) :** *Genetics; Embryology; CUT&RUN; RNA-seq; Immunofluorescence; Vector design and building.*

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

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