2027 Campaign

Student Recruitment

in Maternal and Child Health



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Epigenetic reprogramming linked to pluripotency and germ cell fate

Desired profiles

☐ Internship (CEGEP / undergrad) ☒ M.Sc. ☒ Ph.D. ☒ Postdoc

Research Team

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Bernhard Payer - RQR
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Research Interests

Our lab is interested in the mechanisms and biological roles of epigenetic reprogramming for pluripotency and germ cell/oocyte development. We specifically study the processes of X-chromosome in- and reactivation, classical models of epigenetics, by developing tailored mouse and human iPSC-reprogramming and organoid systems of reproduction. We thereby made fundamental discoveries on the interplay between 3D-genome structure, epigenetics and transcription and the importance of X-chromosome remodeling for meiosis and oogenesis. Furthermore, together with the clinic, we studied the impact of aging on the human oocyte transcriptome by single-cell RNA-Seq and derived patient-specific iPSC-lines and tested their capacity for germ cell differentiation *in vitro*. Our future goal is to further advance our knowledge on epigenetic changes during iPSC-reprogramming and germ cell development *in vitro* and thereby contribute to the

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development of next generation stem cell-based approaches for regenerative and reproductive medicine.

Description of the research project

We have multiple research projects available along the following main research lines. Candidates are invited to specify their preference for one or the other of these sub-projects in their cover letter.

Sub-project 1 - Epigenetic reprogramming and pluripotency:

In our previous work we identified through functional shRNA and CRISPR screens key regulators of X-chromosome reactivation and iPSC reprogramming. For example, we found cohesin to be important to change the 3D-chromatin structure when turning the X-chromosome form an OFF- to an ON-state. Furthermore, we found that inflammatory signaling pathways such as Interferon-gamma (IFNγ) boost X-chromosome reactivation and pluripotency acquisition. Future projects will involve testing if these mechanisms are conserved in other contexts of epigenetic reprogramming *in vitro* and *in vivo*, or if different regulators are at play. Furthermore, it remains to be tested, what is the mechanism of action of the other pathways, which we have identified in our genome-wide CRISPR-screen. The candidate would learn to apply methods such as iPSC-reprogramming, CRISPR engineering of stem cells and single-cell RNA-Seq and epigenomic profiling.

Sub-project 2 - Epigenetic reprogramming and germ cell development *in vitro* and *in vivo*:

Our previous work has shown the importance of X-chromosome dosage control for *in vitro* oogenesis from embryonic stem cells using ovarian organoids. We have thereby identified molecular pathways, which are linked with the X-chromosome state, and which affect the different steps of mouse and human germ cell differentiation *in vitro* or using *in vivo* mouse models. The candidate will use CRISPR engineering to perturb these pathways and test their mechanism for oocyte development. He/she will learn to apply advanced tissue engineering approaches from pluripotent stem cells and study the phenotypes using single-cell and epigenomic analysis methods.

Sub-project 3 – Epigenetic regulation of *in vitro* oogenesis from human pluripotent stem cells:

We have shown that faithful epigenetic remodeling of the X chromosome is critical for differentiation of mouse pluripotent stem cells into oocytes *in vitro*. Human *in vitro* systems however did not reach beyond early oocyte stages so far. A major bottleneck has been faithful epigenetic reprogramming to erase and establish epigenetic marks, which is critical for germ cell maturation, and offspring health *in vivo*.

In this project, the candidate will use human pluripotent stem cells (hPSCs) of different epigenetic states to assess the impact of the epigenome on human germ cell differentiation with the goal to reach more mature oocytes. The project will make use of advanced cell culture models such as ovarian organoids, CRISPR engineering and single-cell expression profiling / multi-omics techniques.

Study programs

Individuals who have completed or are about to complete training in the following areas are invited to apply:

- Reproduction, stem cells, developmental and cell biology, molecular biology, genetics, genomics, or bioinformatics.

Required expertise and skills

The ideal candidates would have experience in some of the following techniques: mammalian cell culture, tissue engineering, flow-cytometry, genomics, microscopy, CRISPR, molecular biology, mouse embryology, bioinformatics.

Personal skills: Curiosity-driven, self-motivated, ambitious, team-player, excellent communication skills in English.

Funding

Masters (M.Sc.): Minimum funding of $ 25,000 CAD per year will be granted to the candidate, until they receive their own financial support through granting agencies or foundations.

Doctorate (Ph.D.): Minimum funding of $ 30,000 CAD per year will be granted to the candidate, until they receive their own financial support through granting agencies or foundations.

Postdoctoral Fellowship: Funding will be adjusted depending on experience and expertise level of the candidate (minimum $ 49,000 CAD per year) and will be granted until they receive their own financial support through granting agencies or foundations.

Keywords

Epigenomics, iPSC-reprogramming, germ cells, organoids, *in vitro* oogenesis, pluripotent stem cells, reprogramming, X-chromosome inactivation

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