Major campaign

Doctoral and postdoctoral recruitment in mother-child health

05 – Epigenetic reprogramming linked to pluripotency and germ cell fate

Type de projet : ☒ Doctoral ☐ Postdoctoral

Research Team

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Research Axis: Fetomaternal and Neonatal Pathologies

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 germ cell and oocyte development. 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 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:

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 prospective student would learn to apply methods such as iPSC-reprogramming, CRISPR engineering of stem cells and single-cell RNA-Seq and epigenomic profiling.

2.) Epigenetic reprogramming and *in vitro* germ cell development:
Our previous work has shown the importance of X-chromosome dosage control for *in vitro* oogenesis from mouse 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 *in vitro* germ cell differentiation. The student 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.

Study programs targeted

The student will be enrolled in the PhD program of Molecular Biology at Université de Montréal.

Required expertise and skills

The prospective student will have a background in the fields of either reproduction, stem cells, developmental biology, molecular biology, genetics, or genomics.
The ideal candidate would have experience in some of the following techniques: mammalian cell culture, tissue engineering, flow-cytometry, genomics, microscopy, CRISPR, molecular biology, bioinformatics.
Personal skills: Curiosity-driven, self-motivated, ambitious, team-player, excellent communication skills in English.

Funding

Minimum funding of 26.500 CAD per year will be granted to the candidate, until they receive their own financial support through granting agencies or foundations.

Keywords

Pluripotent stem cells, germ cells, X-chromosome inactivation, iPSC-reprogramming, organoids, epigenomics, *in vitro* oogenesis

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