Project title	Understanding Embryonic Esophageal and Tracheal Development using Induced Pluripotent Stem Cells		
Study level(s)	☐ MSc	☒ PhD	☐ Postdoctorate
Principal investigator(s)	Christophe Faure		
Project duration	4 years		
Start date	As soon as possible		

Date of posting: 2023-03-10

Esophageal Development and Engineering Laboratory.

During embryonic development, the esophagus and trachea develop from the anterior foregut tube. Disruption in the separation of the AF into two distinct tubes results in foregut malformations such as esophageal atresia and trachea-esophageal fistula (EA/TEF) affecting 1 in 3,500 births. The mechanisms underlying the embryonic and fetal development of EA/TEF are poorly understood. Most of our knowledge on anterior foregut bifurcation and subsequent esophagus development is based on animal models which revealed key genes, molecular pathways and signaling molecules that regulate foregut separation and continue to play key roles in esophagus development and homeostasis. Human pluripotent stem cells (hPSCs) provide an efficient system to model and understand human organ development based on mimicking embryonic developmental stages to generate cell and tissue types originating from all 3 germ layers. Our Lab focuses on the generation of mature esophageal and respiratory epithelium using healthy- and patient-derived induced pluripotent stem cells to better understand the developmental pathways involved in the normal development of the esophagus and trachea. More information available on http://esophaguslab.christophefaure.org/index.html

Research project description.

Our lab has successfully differentiated iPSCs from healthy individuals and EA/TEF patients into mature 3-dimensional esophageal organoids. Key factors SOX2 and NKX2.1 expression were abnormal in the patient-derived anterior foregut and organoids. We hypothesize that a transient dysregulation of SOX2 and the abnormal expression of NKX2.1 in patient-derived cells could be responsible for the abnormal foregut development. This project aims at understanding the mechanisms, in the EA/TEF patient-derived iPSCs, leading to the transitory dysregulation of SOX2 at the anterior foregut stage and the abnormal expression of respiratory markers (NKX2.1) in the esophageal organoids.

Aim 1 will analyze if SOX2 expression in the anterior foregut is regulated by long noncoding RNAs and/or whether SOX2 expression is epigenetically regulated. Such mechanisms could be involved to explain differences in gene expression not seen at the genomic level in EA/TEF patients. **Aim 2** will test the hypothesis that a lower expression of SOX2 in the anterior foregut leads to abnormal esophageal development and abnormal maintenance of esophageal identity by using siRNA in healthy iPSC to transitorily down-regulate SOX2 expression.

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Université de Montréal

Required training and profile.

Highly motivated graduate student with lab research experience and good bench skills.
Applicants should hold a M.Sc. in biomedical sciences, biochemistry, physiology, or cellular or molecular biology.
French and English knowledge is an asset.
Applicant should be trained in:

- Cell culture.
- RT-PCR.
- Immunological methods such as IHC/IF, Flow Cytometry, ELISA
- Experience with iPSCs and single-cell RNA sequencing would be appreciated, but not necessary.

Training will be provided.
Students will participate in scientific and professional courses, lab meetings and journal clubs, and attend national and international scientific conferences.

Conditions.

Winter 2023, open until filled. Successful candidates will be supported by research grants (salary based on CHU Sainte-Justine Research Centre policy) and will be strongly encouraged to apply at various competitions for student fellowship awards.

Submit your application.

Candidates must send the required documents to **Christophe Faure** at christophe.faure@umontreal.ca

Please provide:

√ *Curriculum vitæ*
√ Most recent transcripts
√ Cover letter
√ References

Equity, diversity and inclusion

The masculine gender is used without discrimination and for the sole purpose to facilitate reading. The CHU Sainte-Justine subscribes to the principle of equal access to opportunities and invites women, members of visible and ethnic minorities, persons with disabilities and Indigenous people to apply. We would appreciate it if you could inform us of any disabilities that would require technical and physical accommodation adapted to your situation during the selection process. Please be assured that we will treat this information as confidential.

Studies at the CHU Sainte-Justine Research Center

Pursue your graduate or postdoctoral studies at the **CHU Sainte-Justine Research Center**, and be one of the 500 students, fellows and interns involved in accelerating the development of knowledge in the field of maternal, child and adolescent health, whether in basic or clinical research. Under the supervision of prominent scientists, especially in leukemia, rare pediatric diseases, genetics, perinatology, obesity, neuropsychology and cognition, scoliosis and rehabilitation, you will have the opportunity to work with multidisciplinary scientific teams and collaborators from all over the world.

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About the CHU Sainte-Justine Research Center

CHU Sainte-Justine Research Center is a leading mother-child research institution affiliated with Université de Montréal. It brings together more than 200 research investigators, including over 90 clinician-scientists, as well as 500 graduate and postgraduate students focused on finding innovative prevention means, faster and less invasive treatments, as well as personalized approaches to medicine. The Center is part of CHU Sainte-Justine, which is the largest mother-child center in Canada and the second most important pediatric center in North America. More on research.chusj.org