

## **INTERNSHIP PROJECTS**



#### INTERNSHIP PROJECTS

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Internship project #1

## Regulation of mitotic mechanisms by phosphatases

Under the supervision of Vincent Archambault *Cell Cycle Regulation Research Unit* 

#### **PROJECT DESCRIPTION**

Cancers are caused by disruptions in the mechanisms that control cell proliferation. Understanding cell division in molecular terms helps identify therapeutic targets. To enter mitosis, a cell must break its nucleus, condense its chromosomes, and build a spindle. This transition is triggered by the phosphorylation of several effector proteins by kinases to modify their activities. To complete mitosis, the cell must segregate its chromosomes, reform a nucleus in each daughter cell, disassemble the spindle, and reorganize chromatin. This transition requires the dephosphorylation of several proteins by phosphatases.

The proposed project will aim to understand the roles of specific phosphatases in the regulation of centrosomes or the nucleolus in the mitotic cycle. The fruit fly Drosophila will be used as a highly versatile experimental model. The molecular mechanisms that control cell division are highly conserved between flies and humans. The knowledge acquired will allow us to better understand mitotic defects in cancer cells and could help the development of new therapeutic approaches targeting phosphatases.

The internship project will involve Drosophila culture and genetics, fluorescence microscopy in living or fixed cells and tissues, cell culture, molecular biology and biochemistry. The selected intern will be supervised and will work in a team with a doctoral student and a research associate who are already conducting research on the same topic in our laboratory. The project will be designed to allow the person to acquire a certain autonomy and generate results that can be integrated into a publication.

See the lab's external website (with movies): http://www.archambault.iric.ca

#### LAB TECHNIQUES

Human cell culture Microscopy Molecular Biology Biochemistry Genetics

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/vincent-archambault archambault.iric.ca



Internship project #2

## Characterization of biosensors based on nanoelectronic circuits

Under the supervision of Delphine Bouilly Design and Application of Electronic Nanobiosensors Research Unit

#### **PROJECT DESCRIPTION**

In our laboratory, we work on the development of electronic biosensors for the detection of proteins and nucleic acids. These sensors are made of field-effect transistor (FET) devices based on functionalized conductive nanocarbon materials, such as atomically-thin graphene or carbon nanotubes. Nanocarbon-FETs are a promising technology for the quantitative detection of biomarkers, offering unique advantages such as simplicity, low-cost fabrication and label-free real-time electrical readout. The goal of this internship will be to optimize surface interactions between biological molecules and graphene devices, using a combination of electrical measurements of the nanosensors, high-resolution surface microscopy and/or computational approaches. These experiments will be used to optimize sensitivity metrics of these sensors for the detection of cancer biomarkers.

#### LAB TECHNIQUES

Microfabrication & micro/nanoelectronics Surface chemistry Bioconjugation chemistry High-resolution microscopy Computational methods

#### FOR MORE INFORMATION

https://www.iric.ca/en/research/principal-investigators/delphine-bouilly



Internship project #3

# Study of mechanisms regulating metabolic changes in treatment-resistant breast cancers

Under the supervision of Geneviève Deblois Metabolic and Epigenetic Alterations in Cancer Research Unit

#### **PROJECT DESCRIPTION**

A common feature of aggressive cancers is their ability to tolerate antitumor treatments exposure such as chemotherapy. The development of chemotherapy resistance comes with metabolic changes in the cancer cells. In addition of meeting the energetic, anabolic and antioxidants needs of cancer cells, these metabolic alterations can also affect the cancer cells identity by altering their epigenomes, since chromatin-modifying enzymes are regulated by the abundance of certain metabolites. Therefore, it is essential to understand how cancer cells adapt their metabolism when developing resistance to therapies in order to improve the effectiveness of antitumor treatments. We have identified metabolic changes that promote the survival of breast cancer cells when exposed to certain chemotherapies. Our work suggests that these metabolic adaptations affect some epigenetic modifications of chemoresistant breast cancer cells. The aim of this internship is to better understand the mechanisms that regulate this metabolism reprogramming as well as their consequences on the epigenetic profiles of chemoresistant breast cancer cells. This project will identify new vulnerabilities that could be exploited to better target breast cancers that are resistant to chemotherapy.

#### LAB TECHNIQUES

Molecular Biology Cell Culture Chromatin immunoprecipitation qPCR Metabolic profiling

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/genevieve-deblois



Internship project #4

### **Regulation of collective cell migration by the kinase Misshapen**

Under the supervision of Gregory Emery Vesicular Trafficking and Cell Signalling Research Unit

#### **PROJECT DESCRIPTION**

Collective cell migration is a process involved in morphogenesis during development and is also utilized by cancer cells to disseminate and form metastases. Previous work in our laboratory has characterized the role of the kinase Misshapen (Msn) in coordinating cells during the collective migration of border cells in the Drosophila egg chamber. However, several aspects of Misshapen's function, including how it regulates cell contractility, remain to be understood. The aim of this project is to investigate the interaction between Misshapen and major regulators of contractility by using genetic interactions, highresolution confocal microscopy, and videomicroscopy.

#### LAB TECHNIQUES

Drosophila genetics Confocal microscopy Videomicroscopy

#### POUR PLUS D'INFORMATIONS

iric.ca/research/principal-investigators/gregory-emery



Internship project #5

# Optimization of Metagenomic Analyses for Whole Exome and Whole Genome Sequencing

Under the supervision of Carino Gurjao Genomic and Integrative Medicine Research Unit

#### **PROJECT DESCRIPTION**

Tumor bulk DNA sequencing data has been shown to contain a substantial number of sequencing reads derived from microbial sources, which can be computationally classified to identify microbial taxa. However, this classification process is error-prone due to biological complexities and technical artifacts, and it requires careful, biology-aware interpretation to avoid misclassification.

Student Responsibilities:

- Learn core concepts of genomic and metagenomic analyses, particularly the handling of sequencing reads from WES and WGS datasets.

- Identify and analyze biases introduced by different sequencing approaches (WES vs. WGS) and how these affect the accuracy of metagenomic classification.

- Perform power analyses to estimate the number of microbial reads required for accurate metagenomic detection and classification in both WES and WGS datasets.

- Contribute to the development of robust methods to minimize false positives in microbial

classification, improving data interpretation in tumor sequencing contexts.

#### LAB TECHNIQUES

- Programming in Python or R for data analysis and visualization.

- Familiarity with handling and analyzing high-throughput sequencing data, with a focus on WES and WGS.

- Exposure to statistical methods for power analysis in sequencing-based studies.

#### FOR MORE INFORMATION

New Principal investigator - Expected arrival in early 2025



Internship project #6

# Role of SCL interacting partners for hematopoiesis and leukemia development

Under the supervision of Trang Hoang Hematopoiesis and Leukemia Research Unit

#### **PROJECT DESCRIPTION**

Our laboratory is interested in the molecular mechanisms responsible for the development of hematopoiesis and the formation of acute leukemia. We have identified novel interacting partners of the SCL complex, a multifactorial transcriptional complex acting at multiple levels in the hematopoietic system. The first objective of the project is to confirm in vitro the interaction of the SCL complex members and the newly identified partners by different molecular approaches. In addition, the functional consequences of these interactions will be studied in an ex vivo system reproducing the hematopoietic niche and allowing the differentiation of normal and leukemic primary stem cells.

#### LAB TECHNIQUES

Molecular Biology (qPCR, cloning) Immunoprecipitation Western blot Cell culture (cell lines and primary cells) Flow cytometry Genetics (mouse model)

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/trang-hoang



Internship project #7

# Defining the molecular mechanisms leading to the development of acute leukemia

Under the supervision of Trang Hoang Hematopoiesis and Leukemia Research Unit

#### **PROJECT DESCRIPTION**

We have identified the thymocyte subpopulation that is at the origin of acute leukemia induced by the SCL and LMO1 oncogenes. To generate leukemia, these pre-leukemic stem cells (pre-LSCs) must escape several intrinsic molecular controls acting in the cell. The research project aims in understanding how pre-LSCs manage to bypass these surveillance mechanisms and adapt to oncogenic stress. A better understanding of these mechanisms will lead to the identification of therapeutic vulnerabilities and drugs for specific treatment of leukemia patients.

#### LAB TECHNIQUES

Molecular Biology (qPCR) Cell biology (culture of primary cells) Flow cytometry Genetics (mouse model) Bioinformatics analysis (RNAseq)

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/trang-hoang



Internship project #8

# Cellular models for cancer and regenerative medicine

Under the supervision of David Knapp *Cellular Engineering Research Unit* 

#### **PROJECT DESCRIPTION**

Several projects are available depending on candidate interests. These include modeling concussion and therapies to treat it using human cerebral organoids, modeling leukemia development with the genome engineering of primary human hematopoietic stem cells, and computational modeling of cell differentiation and treatment response in pancreatic tumours. Students (on wet lab projects) will perform live-cell imaging, immunofluorescence, flow cytometry, CRISPR/Cas9 mediated precise genome editing, molecular cloning, stem cell culture. Students interested in computational projects will work with single-cell RNA and ATAC-seq data, classical and AI based gene regulatory network models and agent-based modeling. They will work under the day-to-day direction of a senior PhD student who is directing the project. There will also be opportunities to learn other techniques and contribute to other projects.

#### LAB TECHNIQUES

Cell culture Magnetic cell separation Nucleofection Precise genome editing by CRISPR Live-cell imaging Flow cytometry PCR Gel electrophoresis

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/david-knapp



Internship project #9

## Understanding how adult stem cells divide in vivo

Under the supervision of Jean-Claude Labbé Cell Division and Differenciation Research Unit

#### **PROJECT DESCRIPTION**

How do adult stem cells divide *in vivo*, in response to niche signaling? Answering this question has been challenging, mainly due to the lack of appropriate models to visualize stem cells *in vivo*. We have developed a novel method to image the division of adult stem cells in vivo, using the nematode *Caenorhabditis elegans* (*C. elegans*) as model organism. Genetic analysis has revealed specific pathways and regulators that are essential to coordinate stem cell division during development and aging of the animal. We are seeking motivated individuals to pursue the characterization of some of these regulators, to better understand how they contribute to the regulation of stem cell division, using genetic analysis and high-resolution time-lapse imaging approaches.

#### LAB TECHNIQUES

RNAi Genetic analysis In vivo time-lapse imaging Quantitative image analysis *Caenorhabditis elegans* 

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/jean-claude-labbe



Internship project #10

# Mechanisms of action of full antiestrogens in breast tumor cells

Under the supervision of Sylvie Mader Molecular Targeting for Breast Cancer Treatment Research Unit

#### **PROJECT DESCRIPTION**

About 2/3 of breast tumors express or overexpress the estrogen receptor and its growth is stimulated by estrogen. Anti-estrogens are competitive inhibitors of estrogen receptors. There are two classes of antiestrogens, which act by different mechanisms. The goal of this project is to characterize the mechanisms of action of anti-estrogen such as fulvestrant, a drug used as a second-line therapy for tumors that are resistant to tamoxifen. Our results indicate that anti-estrogens induce SUMOylation of the receptor and its interaction with a chromatin remodeling complex. The goal of the project is to characterize the importance of these effects in the anti-estrogenicity of fulvestrant.

#### LAB TECHNIQUES

Cell culture Western blot Chromatin immunoprecipitation Luciferase assay

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/sylvie-mader



Internship project #11

### Molecular basis of breast cancer heterogeneity

Under the supervision of Sylvie Mader Molecular Targeting for Breast Cancer Treatment Research Unit

#### **PROJECT DESCRIPTION**

Breast cancer is a heterogeneous disease, breast tumors being classified into different subtypes based on expression of specific molecular markers such as estrogen receptor alpha. Our laboratory has identified a group of transcription factors whose differential expression can identify the main breast cancer subtypes. Our current goal is to assess how these transcription factors determine the phenotype of each subtype and to identify therapeutic targets, especially for subtypes that do not currently benefit from targeted therapies.

#### LAB TECHNIQUES

Cell culture Western blot RT-qPCR shRNA/siRNAs CRISPR-Cas9

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/sylvie-mader



Internship project #12

## Integrating modified bases in RNA folding

Under the supervision of François Major *RNA Engineering Research Unit* 

#### **PROJECT DESCRIPTION**

The intern will assist in the development of an RNA folding algorithm that takes modified bases into account.

#### LAB TECHNIQUES

Databases of modified bases, such as MODOMICS. Programming language: Java or Python.

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/francois-major



Internship project #13

## Discovering the key elements for the regulation of gene expression in interactions between microRNAs and mRNAs

Under the supervision of François Major *RNA Engineering Research Unit* 

#### **PROJECT DESCRIPTION**

The intern will assist with data analysis from gene regulation experiments involving microRNAs, considering the secondary and tertiary structures of the duplexes formed between the microRNAs and the targeted mRNAs.

#### LAB TECHNIQUES

Tools for predicting the structure of microRNA:mRNA duplexes Expression databases (RNASeq) Results from CLIP-AGO experiments

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/francois-major



Internship project #14

# Optimization of compounds as potential therapeutic agents

Under the supervision of Anne Marininer *Drug Discovery Research Unit* 

#### **PROJECT DESCRIPTION**

The internship position will be with the Medicinal Chemistry Platform of the Institute for Research in Immunology and Cancer (IRIC) at the Université de Montréal (UdeM). During his/her term, the intern will be working with a team of experienced chemists, under the direct supervision of a Ph.D. and/or M.Sc.-level scientist.

The Medicinal Chemistry Platform has a long-standing research partnership with a major pharmaceutical company and is currently engaged in the hit and lead optimization phases of full drug discovery programs. As part of this effort, the student will have full access to program-related data and proprietary structures. The expectation is that the student will be doing hands-on synthesis at the bench, in order to generate designated target molecules to be submitted for biological evaluation. This will involve all aspects of synthetic organic chemistry, including preparation, isolation, purification and spectral analysis of small molecules in various lead series. The work will also necessitate conscientious record-keeping, in the form of a research notebook, and the effective oral and written communication of research results. In order to further develop an understanding of medicinal chemistry, the student will be encouraged to participate in the critical analysis of structure-activity relationships generated by themselves and others and in devising potential strategies for addressing relevant program issues.

The student will be expected to work effectively within a diverse and multi-site team of collaborators, including chemists, molecular biologists, pharmacologists, toxicologists, CADD specialists, etc. As such, the intern will be exposed to all aspects of the drug discovery process and will have a genuine opportunity to make significant contributions to a promising drug discovery program, all in the context of a unique university-industry alliance.

#### LAB TECHNIQUES

Synthetic organic chemistry: Preparation, isolation, purification and spectral analysis.

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/anne-marinier



Internship project #15

Rewiring of cancer-initiating signals to cell death and senescence pathways as a therapeutic strategy

Under the supervision of Matthew J. Smith Cancer Signaling and Structural Biology Research Unit

#### **PROJECT DESCRIPTION**

The RAS GTPases are fundamental regulators of normal development, causative agents in an extraordinary number of human cancers, and key determinants in several developmental disorders termed RASopathies. RAS proteins are encoded by three proto-oncogenes: HRAS, KRAS and NRAS. Of these, KRAS mutations are most frequent in human cancers, present in 22% of all tumours and 61% of pancreatic, 33% of colon and 17% of lung cancers. These are amongst the most clinically refractory cancers we have today, representing the first, third and fourth leading causes of cancer death worldwide. Despite extensive effort over three decades, there remain no clinically successful drugs that target RAS itself. We thus require new approaches to target these cancer-causing proteins, and current approaches are focus on downstream 'effector' pathways through which RAS transmits its activating signals. Several current therapies target activating pathways via inhibition, but the antithesis of such an approach, rewiring or stimulating pathways that control cell death (apoptosis), should also have efficacy. This internship project will contribute to our work in understanding how RAS interacts with proteins involved in apoptosis and control of cellular senescence. The final objective will be creation of RAS mutants that 'rewire' signaling to effective self-termination, with eventual look to small molecule screens for identification of compounds targeting the characterized mutation sites. To accomplish these aims we need to first characterize how individual RAS and RAS-binding proteins interact in a biochemical and structural sense. The trainee will be involved in cloning, expression and production of these proteins. Upon successful isolation of purified components, we will undergo screens to identify crystallography conditions for eventual structure determination of the RAS-effector complexes. This project will improve our knowledge of RAS biochemistry and biology, with an end goal to better the treatment, diagnosis, and prevention of RAS-driven cancers.

#### LAB TECHNIQUES

Cloning Protein Biochemistry X-Ray Crystallography Tissue Culture

#### FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/matthew-smith