2023 IRIC NEXT GENERATION AWARDS

INTERNSHIP PROJECTS

INSTITUTE FOR RESEARCH
IN IMMUNOLOGY
AND CANCER

IRIC

Université de Montréal

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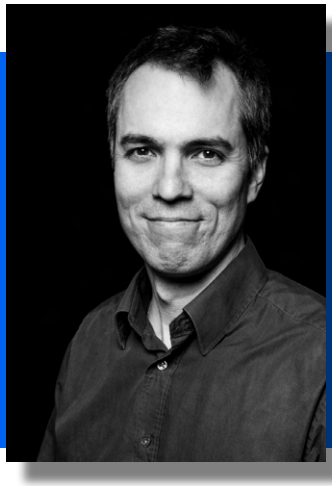


Internship project #1

The molecular mechanisms of cell division

Under the supervision of Vincent Archambault
Cell Cycle Regulation Research Unit

PROJECT DESCRIPTION

Cancer is defined by excessive cellular proliferation. Our laboratory is interested in understanding the molecular mechanisms that control cell division. In mitosis, chromosomes condense and separate on a spindle of microtubules before cytokinesis. The genes and proteins involved are strongly conserved between species and are mutated in cancers. We use cells in culture and the fly Drosophila as models. Our fundamental discoveries improve our molecular understanding of the process of cell division and of its regulation. This knowledge serves as a basis for the design of new targeted anti-cancer therapies that block cell division. The specific subject of the project will depend on what is most exciting in the lab at that time, and the choice will be made also following the student's preferences.

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

LAB TECHNIQUES

Microscopy
Imaging
Molecular Biology
Biochemistry
Genetics

FOR MORE INFORMATION

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

Internship project #2

Characterization of bio/chemical interactions at the surface of nanocarbon-FET biosensors

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 project is to characterize surface interactions between biological molecules and graphene devices, using electrical measurements of the nanosensors and high-resolution surface microscopy. 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

FOR MORE INFORMATION

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

Internship project #3

Study of the epithelial mesenchymal transformation in metastatic cells

Under the supervision of Sébastien Carréno
Cellular Mechanisms of Morphogenesis during Mitosis and Cell Motility Research Unit

PROJECT DESCRIPTION

90% of cancer patients die from abnormal migration of cancer cells (metastasis) throughout the body. The epithelial-mesenchymal transition (EMT) allows cells to acquire the ability to migrate through the body. This process is normally restricted to the development of the embryo and is therefore turned off after birth. However, cancer cells are able to reprogram the TEM to migrate and to form metastases. Understanding how cancer cells reprogram the TEM is therefore an important challenge for fundamental and biomedical research. Our laboratory has discovered a mechanism that blocks the TEM in healthy cells (JCB 2008 JCB 2011 JCB 2013). Our work suggests that cancer cells bypass this mechanism to reprogram the TEM and metastasize. This project aims to better understand the basic mechanism that we have identified and thus better understand how cancer cells are reprogramed. It is of crucial importance since it will allow to define targeted anti-metastatic strategies to fight against cancer.

LAB TECHNIQUES

Molecular biology
Cell biology
Biochemistry
5D time-lapse microscopy

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/sebastien-carreno

Internship project #4

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 #5

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 #6

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 INFO

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 David Knapp
Cellular Engineering Research Unit

PROJECT DESCRIPTION

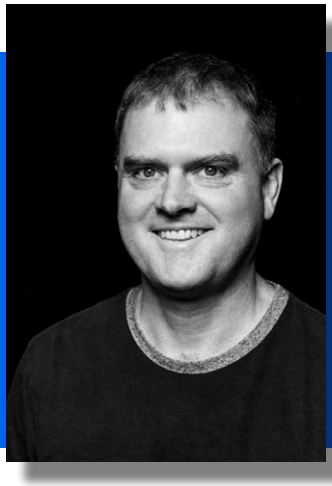
This project focuses on understanding how mutations associated with clonal hematopoiesis interact to cause a progression to leukemia. To study this phenomenon, specific recurrent point mutations associated with clonal hematopoiesis will be introduced alone or in combinations (based on their co-occurrence in leukemia) into normal human hematopoietic stem cells (HSCs). How these mutations/ combinations affect cell function will then be measured through serum-free cultures and stromal co-cultures combined with live-cell imaging and flow cytometry. The student will be involved in the isolation and cryopreservation of progenitors from human umbilical cord blood, genome editing them to introduce the mutations, fluorescence activated cell sorting to isolate the HSC population, and the downstream functional measurements. 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 INFO

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



Internship project #8

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 #9

Implementation of a novel neural network approach to characterize small molecules for drug discovery

Under the supervision of Sébastien Lemieux
Functional and Structural Bioinformatics Research Unit

PROJECT DESCRIPTION

Machine learning approaches have been promising for a long time the ability to predict small molecule activities to accelerate hit identification in drug discovery. Recent advances in deep learning (such as Graph Convolutional Neural Networks, GCNN) are renewing this hope, but so far with relatively limited success in practice. We suspect that the main challenge that these algorithms encounter is the cryptic and incomplete numerical representation used to input small molecules into neural networks. Here, we aim to replace the traditional molecular graph representations (such as molecular fingerprints or GCNN) with expression profiles derived from live human cells exposed to each compound.

To realize this paradigm shift, we will need to develop a high-bandwidth, low-cost solution to experimentally measure complete expression profiles and demonstrate its benefit in predicting active compounds against breast cancer cell lines and AML primary specimen. The profiling method will rely on an innovative split-seq approach, combined with micro-fluidics to rapidly and cost-effectively characterize thousands of small molecules for an estimated cost of 10$ each. With this approach, the cost of profiling would then become much less than the cost of chemical synthesis (estimated between 500-2500$ during a typical drug optimization phase).

Using bioinformatics tools, the trainee will work on publicly available datasets which consist of gene expression profiles for thousands of small molecules at dozens to hundreds of cell lines. The project aims to develop a neural network approach to characterize the trios small molecules, genes, and cell lines. This information helps develop drugs.

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/sebastien-lemieux

Internship project #10

Stage-Specific Regulatory Role of SWI/SNF Subunits in Hemopoietic Development

Under the supervision of Julie Lessard
Chromatin Structure and Stem Cell Biology Research Unit

PROJECT DESCRIPTION

Combinatorial assembly of alternative families of subunits confers functional specificity to ATP-dependent SWI/SNF chromatin remodeling complexes by allowing the recognition of distinct gene targets during cellular differentiation. Recent studies from our lab revealed that some subunits of SWI/SNF complexes are essential for hemopoietic stem cell (HSC) function, while others are required later in the hemopoietic hierarchy for the development of specific lineages (i.e. lymphoid, erythroid or granulocytic-specific functions). The objective of this project is to investigate the function and mechanism of action of a newly identified subunit of these complexes in fetal and adult hemopoiesis.

LAB TECHNIQUES

Molecular biology
Cellular biology
Biochemistry
Mouse models
Bone marrow transplantations
Transfections and lentiviral infections
Gene expression analyses

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/julie-lessard

Internship project #11

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 #12

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 #13

RNA structure prediction from single sequences

Under the supervision of François Major

RNA Engineering Research Unit

PROJECT DESCRIPTION

The trainee will learn about RNA structure and current RNA structure prediction tools based on thermodynamics, probabilities, as well as machine learning. They will be introduced to the tools developed in the lab and be asked to contribute to current projects by either developing new code (in Python or Java), organizing data (for benchmarking), or offer new functionalities and services on the web.

LAB TECHNIQUES

Programming (Python or Java)
Data organization
Data structure
Algorithms.

FOR MORE INFORMATION

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

Internship project #14

MicroRNA interaction networks prediction

Under the supervision of François Major
RNA Engineering Research Unit

PROJECT DESCRIPTION

The trainee will learn about microRNA biogenesis and function. They will be introduced to software tools developed in our lab to predict microRNA interactions with RNA. They will be asked to contribute to current projects by either developing new code (in Python or Java), organizing data (for benchmarking), or offer new functionalities and services on the web.

LAB TECHNIQUES

Programming (Python or Java)
Data organization
Data structure
Algorithms.

FOR MORE INFORMATION

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

Internship project #15

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 #16

Functional implication of selected genetic events in hematopoietic stem cells self-renewal and leukemic transformation

Under the supervision of Guy Sauvageau
Molecular Genetics of Stem Cells Research Unit

PROJECT DESCRIPTION

Next-generation sequencing has greatly refined the genetic and transcriptional landscapes of hematopoietic cells. Newly uncovered mutations and pathways are now thought to play key roles in governing the fate of the hematopoietic system, but until now have not been confirmed experimentally. We now envision to functionally test the implication of some of these genetic events in the self-renewal of hematopoietic stem cells as well as in the induction of acute leukemia transformation.

The selected student will actively participate in every stages of the project, from the molecular sub-cloning of candidate genes, the production of transducing viral particles, the handling of primary human samples to the final analysis of hematopoietic cell biology using well-established cell-based assays.

Along the way, recent genetic engineering technologies such as shRNA and CRISPR shall be implemented to knock-down additional transcripts of interest in various cell systems (cord blood cells, AML cell lines, primary AML cells) to assess their molecular functions in acute myeloid leukemia progression and stem cell biology.

LAB TECHNIQUES

Cell culture
Flow cytometry
Cloning
qPCR

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/guy-sauvageau

Internship project #17

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

Internship project #18

SUMO-regulated cell functions in human health

Under the supervision of Pierre Thibault
Proteomics and Mass Spectrometry Research Unit

PROJECT DESCRIPTION

The small ubiquitin-like modifier (SUMO) protein is an ubiquitin-like (UBL) protein that is highly dynamic and can reversibly target lysine residues on a wide range of proteins involved in several essential cellular events, including protein translocation and degradation, DNA damage response, cell cycle progression, cell differentiation and apoptosis. The Protein Inhibitor of Activated STAT (PIAS) enzymes are E3 SUMO ligases that plays important roles in various cellular pathways, including the coordination of cell processes, such as gene expression, the DNA damage response and inflammation. To understand the mechanism of action of SENPs, we will use a quantitative SUMO proteomic approach to identify potential SENP substrates in a system-wide manner. We will also study the effects of SENP knockout on the proliferation and migration of cells.

LAB TECHNIQUES

Cell culture,
Microscopy
Affinity chromatography
Proteomics
Mass spectrometry

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/pierre-thibault

Internship project #19

Identification of the histological correlates of ferroptosis signatures in pancreatic cancer

Under the supervision of Vincent Q. Trinh
Digital histology and advanced pathology Research Unit

PROJECT DESCRIPTION

Ferroptosis is a form of cell death which has been associated to prognosis. There is extensive publicly available data which has not been mined for ferroptosis signatures in the pancreas. The project consists in datamining the Cancer Genome Atlas for ferroptosis signatures and identifying histological (pathology) correlates of these signatures. The student will participate in marker selection, in datamining, in analyzing RNA-seq data, analyzing associated slides, correlating with clinical data, and correlating with pathology slides.

LAB TECHNIQUES

R
Data extraction
Data analysis
Statistical correlation with clinical data in SPSS
Pathology review of slides

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/vincent-q-trinh

Internship project #20

Multiplex imaging of dysplastic stem cell populations in pancreatic precursors

Under the supervision of Vincent Q. Trinh
Digital histology and advanced pathology Research Unit

PROJECT DESCRIPTION

Single-cell RNA-seq data show cellular diversity in pancreatic precursor tumors. Trajectory analyses identify dysplastic stem cells represent the reservoir of cells eventually transforming into invasive cancer. DSCs have not been studied in preinvasive stages of disease in the pancreas. By using novel multiplex imaging approaches, the student will analyze human pancreas tissue for these populations and correlate their burden to disease progression.

LAB TECHNIQUES

R
Slide staining
Slide scanning
Image co-registration in MATLAB
Image analysis in Ilastik and CellProfiler
Correlation with clinical data in SPSS

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/vincent-q-trinh

Internship project #21

Defining the molecular mechanism of action of novel compounds on acute myeloid leukemia cells

Under the supervision of Brian Wilhelm
High-Throughput Genomics Research Unit

PROJECT DESCRIPTION

The intern will work with lab members (grad students/research assistant) to characterize the molecular mechanism by which specific drugs block the growth of leukemia cells. Acute myeloid leukemia develops when normal blood stem cells acquire mutations that prevent them from either dying or differentiating. As a result, the progenitor cells continue to grow in the bone marrow blocking normal hematopoiesis. We have recently performed a small molecules screen using 12,000 compounds against 20 patient and model AML samples and have identified a small number of compounds that block AML growth but do not affect normal blood stem cells. We are now looking at these compounds individually to try and understand what they target in the cell and how this prevents the AML cells from growing. This work typically involves treating cells with individual drugs, monitoring specific protein levels or activities or gene expression levels. Because each compound may be acting differently, and on different cellular targets, a range of different approaches must generally be used to elucidate the nature of the anti-AML activity of the drugs.

LAB TECHNIQUES

Cell culture
PCR
Western blotting
NGS analysis
qRT-PCR
Standard molecular cloning

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/brian-wilhelm