

INTERNSHIP PROJECTS



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Project # 1	Regulation of mitotic mechanisms by phosphatases Under the supervision of Vincent Archambault	p. 3
Project # 2	Characterization of biosensors based on nanoelectronic circuits Under the supervision of Delphine Bouilly	p. 4
Project # 3	Validating FPR2 signaling profiles after pro- and anti-inflammatory stimulation with agonists Under the supervision of Michel Bouvier	p. 5
Project # 4	Study of mechanisms regulating metabolic changes in therapy resistant breast cancers Under the supervision of Geneviève Deblois	p. 6
Projets # 5	Optimization of Metagenomic Analyses for Whole Exome and Whole Genome Sequencing Under the supervision of Carino Gurjao	p. 7
Project # 6	Role of SCL interacting partners for hematopoiesis and leukemia development Under the supervision of Trang Hoang	p. 8
Project # 7	Defining the molecular mechanisms leading to the development of acute leukemia Under the supervision of Trang Hoang	p. 9
Project # 8	Cellular models for cancer and regenerative medicine Under the supervision of David Knapp	p. 10
Project # 9	Computational mixology: building complex cellular responses from a minimal vocabulary of small molecules Under the supervision of Sébastien Lemieux	p. 11
Project # 10	Mechanisms of action of chemotherapeutic agents used for cancer treatment Under the supervision of Sylvie Mader	p. 12
Project # 11	Optimization of compounds as potential therapeutic agents Under the supervision of Anne Marinier	p. 13
Project # 12	Rewiring of cancer-initiating signals to cell death and senescence pathways as a therapeutic strategy Under the supervision of Matthew J. Smith	p. 14



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

iric.ca/en/research/principal-investigators/delphine-bouilly



Internship project #3

Validating FPR2 signaling profiles after pro- and anti-inflammatory stimulation with agonists

Under the supervision of Michel Bouvier Molecular Pharmacology Research Unit

PROJECT DESCRIPTION

The project focuses on the signaling pathways involved in the regulation of inflammation by the G protein-coupled receptor FPR2 (n-formyl peptide receptor 2). We have identified differences in signaling between pro- and anti-inflammatory ligands using BRET (Bioluminescence Resonance Energy Transfer) technology. Only anti-inflammatory ligands can promote the internalization of the receptor, and there appear to be $G\alpha$ pathways specific to pro-inflammatory ligands.

The aim of the internship will be to confirm that the $G\alpha$ pathways identified by BRET are responsible for the pro- or anti-inflammatory responses observed in immune cells differentiated into macrophages, using molecular biology techniques (RT-qPCR, ELISA), pharmacological inhibitors and genetic manipulations.

LAB TECHNIQUES

Flow-cytometry RT-qPCR ELISA Cell culture

POUR PLUS D'INFORMATIONS

iric.ca/en/research/principal-investigators/michel-bouvier



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

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

iric.ca/en/research/principal-investigators/carino-gurjao



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

Computational mixology: building complex cellular responses from a minimal vocabulary of small molecules

Under the supervision of Lemieux
Functional and Structural Bioinformatics Research Unit

PROJECT DESCRIPTION

Could a small, carefully selected panel of compounds capture the functional diversity of drug-induced transcriptional responses? In this project, you will explore the hypothesis that combinations, in precise proportions, of 32 to 64 carefully selected compounds can approximate the gene expression responses of thousands of others in a cancer cell line, using a single well-characterized model such as MCF7 or PC3. Using the LINCS L1000 dataset, and a fixed nonlinear model of drug dose-response based on the Loewe additivity principle, you will evaluate how well combinations of selected compounds can mimic the effects of all others and determine how many are needed to span the biologically reachable response space.

You'll work with compact representations of gene expression data, learned using neural networks, that remove redundancy and make the analysis more tractable. Using these representations, you'll simulate how drug mixtures behave under a well-established model of additive effects (Loewe), and test how well small subsets of compounds can recreate the effects of many others. The ultimate goal of the internship is to design an experiment-ready validation panel: a set of complex mixtures predicted to induce a wide range of distinct responses, ready to be tested in a future lab experiment. Along the way, you'll generate and analyze a library of thousands of candidate molecules and learn how to evaluate which ones are likely to be the most biologically informative.

This project is ideal for students with prior programming skills, in any language, and an interest in large-scale data analysis, AI, and computational biology. Prior experience with the Julia programming language or neural networks is not needed, our lab has good expertise in both and we love to get interns started with these tools. All the codes you'll need to work with the LINCS dataset are already available in the lab, and the project involves no wet-lab work. If you're excited by the challenge of learning how cells respond to combinations of molecules, and figuring out how to reduce that complexity, this project will offer a clear, well-scoped research experience with lots of room for creativity.

LAB TECHNIQUES

Julia programming language; Large-scale data analysis

FOR MORE INFORMATION

iric.ca/en/research/principal-investigators/sebastien-lemieux https://www.lemieux.iric.ca/



Internship project #10

Mechanisms of action of chemotherapeutic agents used for cancer treatment

Under the supervision of Sylvie Mader

Molecular Targeting for Breast Cancer Treatment Research Unit

PROJECT DESCRIPTION

Drugs used to treat cancer often have complex mechanisms of action and undesirable side effects. In addition, resistance mechanisms specific to cancer cells can limit their effectiveness at suppressing the proliferation and survival of these cells. CRISPR-Cas9 chemogenomic screens performed in cancer cell models can identify drug sensitivity and resistance genes by suppressing the expression of each gene in the genome in cell populations treated or untreated with these molecules and identifying guide RNAs enriched or lost in surviving cells. This approach can thus identify drug mechanisms of action and possible resistance pathways.

The intern will be responsible for validating targets identified during such screening campaigns using CRISPR-Cas9 or shRNA technologies to suppress/decrease the expression of candidate genes and experimental approaches to test the expression and function of these targets as well as the impact of their suppression on cancer cell proliferation and survival.

LAB TECHNIQUES

Recombinant DNA techniques CRISPR-Cas9 knock-out Cell culture Flow cytometry Proliferation and survival assays

FOR MORE INFORMATION

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



Internship project #11

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 #12

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