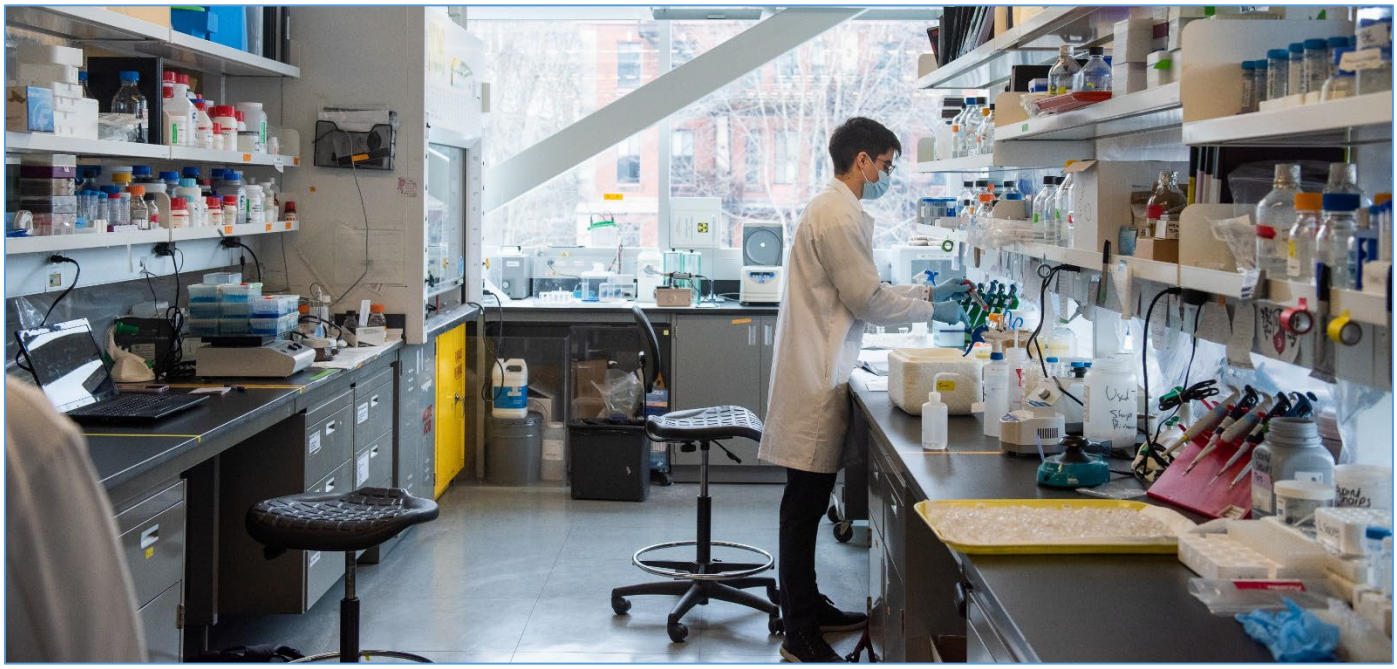
The McGill Biomedical Research Accelerator



2023 Summer Project List

McGill | School of Biomedical Sciences | École des sciences biomédicales

McGILL BIOMEDICAL RESEARCH ACCELERATOR
2023 Summer Projects

Anatomy and Cell Biology

Regulation of telomere maintenance

Supervisor: Chantal Autexier, PhD
Department of Anatomy and Cell Biology
Department of Medicine, Division of Experimental Medicine
Senior Investigator, Lady Davis Institute

Project Description:

Possible projects consist of determining the role of replication stress or of unique regions of telomerase holoenzyme components in telomere maintenance using advanced molecular and cellular biology approaches providing undergraduate students with an opportunity to contribute to and understand how scientific research is conducted. Students recruited to a graduate program will acquire a comprehensive skill set, including teaching, communication, problem-solving and critical analysis that is relevant to varied careers.

Our lab uses fluorescence microscopy and chromatin immunoprecipitation to study telomeres and telomerase recruitment to telomeres. We also use traditional molecular biology approaches such as cloning, degron-mediated protein depletion, real-time quantitative PCR, fluorescence activated cell sorting, RNA and protein immunoprecipitation to identify and characterize the molecular mechanisms controlling telomerase RNA processing, telomerase ribonucleoprotein biogenesis and function at telomeres and in cellular survival and immortalization.

For more information:

http://www.ladydavis.ca/en/autexierlab

Identifying critical steps in ribosome biogenesis for antimicrobial discovery

Supervisor: Joaquin Ortega, PhD
Department of Anatomy and Cell Biology
Centre de recherche en biologie structurale

Project Description:

Antimicrobial resistance is on track to become the next global pandemic. Developing novel antibiotics that target unexplored cellular processes not susceptible to existing resistance mechanisms is urgent. Our laboratory focuses on the assembly process of the bacterial ribosome, which is not currently targeted by any antibiotic. Ribosomes synthesize all cellular proteins. If an organism cannot make ribosomes, it dies. Ribosomes are complex molecular nanomachines made up of over 50 components. We found that critical steps within the ribosome assembly process have tremendous potential as targets for developing novel antibiotics. We are using cryo-electron microscopy to directly visualize and mechanistically understand these critical maturation steps. Uncovering these critical steps in the assembly process will allow leveraging ribosome biogenesis factors as a novel antimicrobial target and discovering new antibiotics that will help curve the rapidly emerging threat of antimicrobial resistance.

For more information:

https://www.joaquinortegalabonlinemcgill.com/

Biochemistry

Muscle stem cell dysfunction in Duchenne muscular dystrophy

Supervisor: Natasha Chang, PhD
Department of Biochemistry
McGill Regenerative Medicine Network

Project Description:

Muscle stem cells are muscle-resident adult stem cells that support the remarkable regenerative capacity of muscle throughout life. Research in our lab is focused on understanding the molecular mechanisms that regulate muscle stem cell function during homeostasis and regeneration. Dysregulation in these mechanisms lead to reduced stem cell regenerative capacity and leads to muscle degeneration. We study how muscle stem cells in Duchenne muscular dystrophy, a lethal genetic muscle disease, are impacted and how their impairment contributes to disease progression. Our lab uses biochemistry combined with cell biology approaches to address fundamental questions in muscle stem cell biology. The student will gain exposure to a wide range of experimental techniques ranging from primary cell isolation from mice to immunocytochemistry and molecular-based assays to study gene and protein expression. The student will also gain experience working within a research team, and develop skills in project management, scientific writing and communication.

For more information:

https://natashachanglab.com/

Pseudophosphatases, cysteine phosphorylation, and cancer

Supervisor: Kalle Gehring, PhD
Department of Biochemistry
Centre de recherche en biologie structurale

Project Description:

Our research focuses on phosphatases involved in cell signaling and metastatic cancer. Phosphatases of regenerating liver (PRLs) are a family of highly oncogenic protein phosphatases. In our laboratory, we determined the first 3D structure of a PRL phosphatase and proved that they function as pseudophosphatases regulating magnesium efflux. Our laboratory uses biophysical and biochemical techniques (X-ray crystallography, NMR, and cryoEM) to decipher the 3D structures of proteins. From snapshots of proteins in different conformations, we can design experiments to decipher their function and how to control them with small molecules or drugs. The student will participate in a research project under the supervision of a senior member of the group. He/she will be taught the different techniques used in the laboratory, how to design a good experiment, and how to present research results. This opportunity will be an excellent preparation for students interested in graduate or professional schools.

For more information:

https://www.gehringlab.net/

Structure-function studies of DNA repair complexes

Supervisor: Alba Guarné, PhD

Associate Director, School of Biomedical Sciences

Department of Biochemistry

Centre de recherche en biologie structurale

Project Description:

We combine integrative structural biology approaches with biochemistry and genetics to study how proteins detect DNA damage and repair it. Genome integrity depends on DNA repair proteins being able to identify damage regardless of sequence context. To this end, many repair enzymes bind DNA lesions in a sequence independent, but structure-dependent manner. In this summer project, students will be paired with a graduate student to study how structure-specific DNA nucleases identify and remove DNA lesions.

For more information:

https://albaguarne.wixsite.com/guarnelab-mcgill

A Chemical Biology Approach to Expanding the Targeting Range of Rocaglates – Potent Anti-Cancer Compounds that Inhibit Translation.

Supervisor: Jerry Pelletier, PhD

Department of Biochemistry

Centre de recherche en biologie structurale

Project Description:

We have identified and characterized a class of compounds, known as rocaglates, that target eukaryotic initiation factor (eIF) 4A to inhibit translation. Rocaglates act as molecular clamps - interacting with both eIF4A and RNA. eIF4A is a member of a family of 35 RNA helicases, many of which are poorly characterized. We have molecular insight into the binding of rocaglates to eIF4A and RNA as the crystal structure has been published and several other RNA helicases have a similar rocaglate binding site, but with subtle amino acid changes. The goal of this project is to screen a library of >200 rocglates for their ability to bind to other helicases – thus identifying molecular probes that can be used to elucidate their function. The project will involve generating retroviruses expressing said helicases, using these to generate unique cell lines, and undertaking cell-based assays to determine rocaglate sensitivity and effect on gene expression.

For more information:

http://www.jerrypelletierlab.com/

Nonribosomal peptide biosynthesis

Supervisor: Martin Schmeing, PhD
Department of Biochemistry
Centre de recherche en biologie structurale

Project Description:

Nonribosomal peptide synthetases (NRPSs) are large microbial enzyme that synthesize natural small molecules that can be used as antibiotics, anticancers and other medicines. We wish to understand how NRPSs act to make these important small molecules. The project is multidisciplinary, using a wide variety of molecular biology, chemical biology, biophysical and structural biology techniques to best understand biosynthesis by NRPSs and give students experience with many experimental approaches.

For more information:

http://www.med.mcgill.ca/biochem/schmeinglab/Schmeing_Lab_website/Home.html

Uncovering molecular mechanisms that protect cells from threats derived from global warming

Supervisor: Maria Vera Ugalde, PhD
Department of Biochemistry
Centre de recherche en biologie structurale

Project Description:

The advancement of global warming evidences the need to be prepared for frequent waves of extremely hot temperatures. This project aims to explore unconventional molecular mechanisms activated to preserve genome integrity and guarantee cell survival after heat exposure. The dedicated cell mechanism to protect cells from heat-stress is known as the heat shock response (HSR). Decades of investigation on the HSR have provided deep knowledge on the induction and cytoplasmic actions of the inducible heat shock protein, HSP70, which copes with protein damage. However, the impact of heat stress on the regulation of protein synthesis during stress is not that well understood. Using the yeast saccharomyces cerevisiae as a model organism, we found that the ribosomal protein Asc1 is essential for survival to heat stress. In this project, we will investigate how Asc1 promotes resistance to heat stress by regulating the translation machinery and selecting specific mRNAs to be translated or degraded.

For more information:

http://www.veraugaldelab.net/

Biomedical Engineering

3D-printed Microfluidic ELISA for the Colorimetric Detection of Anti-Cytokine Auto-Antibodies at the Point-of-Care

Supervisor: David Juncker, PhD
Chair, Department of Biomedical Engineering
McGill Regenerative Medicine Network

Project Description:

Interferons (IFNs) are released by immune cells to trigger anti-viral and immunomodulatory events. Some patients develop auto-antibodies (AAbs) against IFNs to neutralize their functions; these were found in 10-15% of severe COVID-19 cases, resulting in hypoxemic pneumonia and ~1 million deaths (Nature 595.7866 (2021): 283-288; Science 370.6515 (2020): eabd4585). Current methods of anti-IFN AAb detection rely on microplate enzyme-linked immunosorbent assays (ELISAs), which are limited to centralized facilities, leading to lengthy turnaround times, labour-intensive protocols, and costly peripheral equipment, thus prompting the need for an inexpensive and portable point-of-care solution. We propose a 3D-printed microfluidic ELISA with colorimetric detection based on our COVID-19 serology test (Nature 605.7910 (2022): 464-469) for the autonomous detection of anti-IFN AAbs. The device will be adapted to a whole blood immunoassay with instrument-free on-chip liquid handling and pre-programmed reagent delivery honing laboratory-grade performance. The project will include 3D-printing microfluidic designing, assay optimization, and clinical validation.

For more information:

https://juncker.lab.mcgill.ca/

In vitro characterization of conformal nanocoating for human pancreatic islet encapsulation

Supervisor: Maryam Tabrizian, PhD
Department of Biomedical Engineering
McGill Regenerative Medicine Network
Centre for Biorecognition and Biosensors

Project Description:

Transplantation of donor islets has been recently proposed as a long-term treatment option for Type 1 diabetes (T1D) and encapsulation of these islets to prevent implant rejection has been a recent focal point in biomaterials research. In our lab, we have developed a novel nano-coating protocol for encapsulation of single islets and shown that the cells can maintain viability as well as insulin secretion. The current summer student project will build on these findings by assessing the degradation of the coating overtime in vitro using simulated body fluid and measuring the presence of polymers in the supernatant using HPLC, mass spectrometry, and fluorescence spectrophotometry. The project will also look at cellular responses to the nanocoating, namely if there are any transcriptional changes in coated islets, using qPCR, as well as measurement of Intracellular calcium concentration using fluorescent calcium probes.

For more information:

https://tabrizian.lab.mcgill.ca

Goodman Cancer Institute

Mapping protein-binding sites on the HOTAIRM1 long non-coding RNA (lncRNA)

Supervisor: Josée Dostie, PhD

Rosalind and Morris Goodman Cancer Institute

Department of Biochemistry

Project Description:

LncRNAs are a class of regulatory transcripts larger than 200 nucleotides with little coding potential. They are transcribed by RNA polymerase II, but are more cell-type specific and their gene number is far greater than mRNAs. Though key lncRNA roles are emerging in diverse physiological processes and in disease, very little is known about them.
Structure-function analysis is an effective approach towards elucidating underlying mechanisms of RNA transcripts. We suggest mapping binding sites of proteins known to bind HOTAIRM1 – an lncRNA important for cell differentiation acting either as an oncogene or tumour suppressor depending on cancer type. The student will use two approaches to map domains binding the HOXA1 transcription factor or SUZ12 polycomb group protein: 1. In-vitro transcription of existing HOTAIRM1 truncation mutants, followed by incubation and pull-down in NT2-D1 or NB4 cell extracts. 2. Transfection of the HOTAIRM1 mutants, followed by pull-down in the same cancer cell models.

For more information:

https://www.mcgill.ca/biochemistry/about-us/department/faculty-members/dostie

Assess the importance of Chi3L1 cytokine in Mammary tumor progression

Supervisor: William Muller, PhD
Rosalind and Morris Goodman Cancer Institute
Department of Biochemistry

Project Description:

With the rise of immunotherapies as a treatment for various cancers, the need to understand how cancers evade the immune system is at an all-time high. We have uncovered a critical Stat3 regulated cytokine, known as Chi3L1, which is highly expressed in metastatic breast cancers and plays a pivotal role in sculpting the Tumor Immune Microenvironment (TIME).

The main objective of this project is to evaluate Chi3L1 as a potential novel therapeutic target that, when neutralized alone or in combination, will attenuate both primary tumor development and subsequent dissemination to other metastatic sites. We hypothesize that Chi3L1 promotes metastatic breast cancer progression through a combination repolarizing both adaptive and innate immune cells into a pro-tumorigenic state and simultaneously spatial excluding anti-tumor response from the primary tumor site.

Using Genetic Engineered Mouse Model of Luminal B breast cancer, we will evaluate whether genetic ablation of Chi3L1 is sufficient to promote immune elimination of nascent mammary tumors. To test this hypothesis, we have crossed our Luminal B MIC GEMM to the Chi3L1 deficient mice to generate female cohorts of Chi3L1 proficient and deficient mice which, following doxycycline induction, will be monitored for mammary tumor induction and lung metastasis.

For more information:

https://www.themullerlab.com/

Mapping protein-binding sites on the HOTAIRM1 long non-coding RNA (lncRNA)

Supervisor: Alain Nepveu, PhD

Rosalind and Morris Goodman Cancer Institute

Department of Biochemistry

Project Description:

We have identified transcription factors that function as accessory factors that stimulate the activities of base excision repair enzymes. In cancer cells that produce excess reactive oxygen species, these factors are required to accelerate the repair of oxidative DNA damage, thereby preventing cellular senescence and enabling continued proliferation. In vitro, we perform multiple DNA repair assays with purified proteins to define the smallest peptide that can still stimulate enzymatic activity. In cells, we investigate the effect of transcription factor knockdown on genomic DNA damage and DNA repair, and verify that ectopic expression of a small peptide, competent in DNA repair but devoid of transcriptional activity, can rescue the phenotype. In cancer cells, we assess the synthetic lethality of transcription factor knockdown. Our goal is to identify and validate therapeutic targets for future therapeutic interventions in cancer treatment.

For more information:

https://www.mcgill.ca/gci/alain-nepveu-phd

Dissecting the myeloid microenvironment of glioblastoma

Supervisor: Daniela Quail, PhD

Rosalind and Morris Goodman Cancer Institute

Department of Physiology

Project Description:

Macrophages are the dominant immune cell type in glioblastoma and their accumulation is associated with more aggressive disease. Macrophages in the brain are comprised of tissue-resident microglia (yolk-sac derived), and monocyte-derived macrophages (MDM; recruited from the peripheral circulation). These MDM arise from at least 2 developmental trajectories; however, the functional contribution of distinct MDM subsets to glioblastoma progression remains unknown. This project will explore how MDM from distinct progenitor populations influence glioblastoma biology. Students will gain technical experience with preclinical cancer models, cell culture of primary cells from mice, and ex vivo co-culture assays. Flow cytometry and histology will be central techniques that are used to assess anti-tumor immunity.

For more information:

https://quaillab.ca

Development and evolution of the female reproductive tract and ovarian cancer carcinogenesis

Supervisor: Yojiro Yamanaka, PhD
Rosalind and Morris Goodman Cancer Institute
Department of Human Genetics

Project Description:

1. Developmental mechanisms of the female reproductive tract and its evolution in vertebrates.

2. Unique roles of oviduct epithelial regionality in reproduction and its link to ovarian cancer initiation.

3. The role of tissue residential macrophages in ovarian cancer initiation and metastasis

For more information:

https://yojiroyamanaka.wixsite.com/website-1

Human Genetics

A role for the C14ORF39/SIX6OS1 protein in DNA repair

Supervisor: Raquel Cuella-Martin, PhD

Department of Human Genetics

Project Description:

Safeguarding genomic stability is essential to preserve cellular viability. The protein BRCA1 is implicated in the repair of DNA double-strand breaks, and germline heterozygous mutations are associated with breast and ovarian cancer predisposition. Recently, C14ORF39/SIX6OS1 was identified in a CRISPR-KO screen looking for factors that synergize with BRCA1 heterozygous mutations in promoting exacerbated cellular proliferation in mouse cells. C14ORF39/SIX6OS1 is an element of the synaptonemal complex involved in chromosome synapsis at meiotic recombination. However, only a handful of publications describe this gene, and our results suggest a potential synergy with BRCA1 mutation in the tumorigenesis process. We will use CRISPR-dependent base editing to engineer normal ovarian cell lines to insert BRCA1 heterozygous mutations and characterize them using amplicon sequencing and immunoblotting. Using these models, we will explore the effect of C14ORF39/SIX6OS1 loss-of-function in cellular proliferation by high-throughput microscopy.

For more information:

https://www.mcgillgenomecentre.ca/investigators/raquel-cuella-martin/

Genetic Network Rewiring Between Distantly Related Yeast Species

Supervisor: Elena Kuzmin, PhD
Department of Human Genetics
Goodman Cancer Institute

Project Description:

An outstanding question in the field, is the extent of genetic interaction network conservation. We will use trigenic synthetic genetic array methodology in yeast to interrogate complex genetic interaction network rewiring between distantly related yeast species and integrate the findings with other species. This approach will enable us to determine whether genetic network rewiring involving complex genetic interactions can expand the level of conservation of genetic interactions between evolutionary distant organisms.

For more information:

https://kuzmin-lab.github.io/research/

Tumour suppressive network of large chromosomal deletions in triple negative breast cancer

Supervisor: Elena Kuzmin, PhD
Department of Human Genetics
Goodman Cancer Institute

Project Description:

The characterization of large chromosomal aberrations in cancer is an important step in understanding cancer genome evolution and devising novel therapeutic strategies. Cancer genomic analyses showed that certain regions are preferentially lost or gained indicating that these events are selected because they are advantageous during cancer progression. However, functional consequences of large chromosomal deletions have gone relatively unexplored. In this project we will investigate how perturbations of genes within a large chromosomal deletion in triple negative breast cancer can impact cancer initiation and progression by constructing mutant cell lines using CRISPR-Cas system and measure their effect on cell proliferation, apoptosis and cell transformation. We will also assess how pairwise combinations of genes interact to enhance proliferation.

For more information:

https://kuzmin-lab.github.io/research/

Computational pipelines and web-based tools for genetic studies

Supervisor: Daniel Taliun, PhD
Department of Human Genetics
Quantitative Life Sciences

Project Description:

My team develops computational methods, pipelines and analytical web-based tools for gene-disease association analyses using whole genome sequencing data. We use Python, C/C++, Java, and JavaScript with state-of-the-art web development frameworks (such as Vue.js) and workflow managers (such as Nextflow). We utilize large Linux-based high-performance computing clusters with hundreds of CPUs for our data analyses. Currently, we have >10 projects to which you could contribute, learn more about human genetics and disease, and test your programming skills to the fullest.

For more information:

https://dtaliun.github.io/

Genetics of Reproductive Failure

Supervisor: Rima Slim, PhD
Department of Human Genetics
Department of Obstetrics & Gynecology
Division of Experimental Medicine, Department of Medicine

Project Description:

In my laboratory we use next generation sequencing to identify novel causative genes for various forms of reproductive loss. Then, we elucidate the mechanisms by which mutations in these genes lead to these conditions. The overarching goal of this work is to help couples and patients with these conditions by offering them better counselling and assisted reproductive technology services tailed to their exact gene defect. In short, our project aims at using precision medicine to help couples with a genetic etiology underling their condition. The methods we use include patients' recruitment, DNA extraction, cell line establishment, exome sequencing, analysis of exome data, prioritization of candidate genes using in silico tools, validation of selected variants by PCR amplification and Sanger sequencing, investigating the segregation of the variants with the disease phenotype in families, search for other patients with defects in the same genes. All these methods are well-mastered by our laboratory and have been used in previous publications. Some of them are easy and can be learned and mastered in a short time by young trainees. The trainees will also get to familiarize themselves with more sophisticated methods, be initiated to them, and develop a global picture of state-of-the-art human genetic approaches that can be applied to any medical discipline.

For more information:

https://www.mcgill.ca/rslimlab/

Genetically supported circulating proteomics in disease biomarker identification

Supervisor: Sirui Zhou, PhD
Department of Human Genetics
McGill Genome Centre

Project Description:

Circulating proteins represent desirable biomarkers, which are accessible for drug binding, modifiable by therapeutics and lifestyle, and relatively easy to measure. The circulating proteome provide evidence linking genome and disease, reflecting disease pathogenesis happening in specific tissues. Recent technological advances enable high-throughput quantification of thousands of circulating proteins, which can be used as evidence of drug targets, particularly, if the evidence is also supported by genomics. In this project, we will apply a genetic epidemiological framework combining post-GWAS methods such as Mendelian randomization and polygenic risk score to leverage the proteo-genomic map from several large cohorts, followed by validation in biobank data with individual level proteomic measurements (BQC19, UK Biobank and CLSA), to pinpoint protein biomarkers for human diseases.

For more information:

https://cerc-genomic-medicine.ca

Microbiology and Immunology

Circadian rhythms in physiology: implications for infectious diseases and psychiatric disorders

Supervisor: Nicolas Cermakian, Ph.D.
Department of Microbiology and Immunology
Department of Psychiatry
Department of Physiology
Douglas Research Centre

Project description:

Various aspects of physiology present 24h rhythms, due to circadian clocks located throughout the body. Dysregulation of these rhythms can lead to various health issues including mental disorders or cancer. Research in the laboratory aim at defining how circadian clocks control physiology and the implications for disease. Projects include: 1) The circadian control of immune responses: to decipher the mechanisms behind the 24h rhythms of response to pathogens and efficacy of vaccination; 2) The association of circadian disruption with schizophrenia: to understand the reasons why patients with schizophrenia often display sleep problems, and whether such problems can constitute a risk factor for the disease; 3) The identification of new clock genes: to unravel new core mechanisms of the clock, at the basis of rhythmic physiology and behaviour. Experimental approaches in the lab include molecular biology, immunology approaches, neuroanatomy, behavioural analysis. As part of the MBRA internship, the student will work on a project related to one of the above topics.

For more information:

http://ncermakianlab.mcgill.ca

Touching and feeling tissue topology by immune cells as they move

Supervisor: Judith N. Mandl, Ph.D.
Department of Microbiology and Immunology
Department of Physiology
Research Centre on Complex Traits (MRCCT)

Project description:

Immune cells are continuously moving between and within organs to perform their function, navigating tissues with distinct microarchitectures and stiffness. We are interested in how immune cells sense their mechanical environments, how such touch-sensing informs their decision-making as they squeeze past obstacles, and their survival in diverse tissues. In this project you will probe how different primary murine immune cells (from neutrophils to T cells) sense the stiffness of their environment, whether mechanosensors are important in their migration through tight tissues, and what goes wrong when their sense of touch is impaired.

For more information:

http://jmandl.lab.mcgill.ca/

Phase transitions and pandemic virus replication

Supervisor: Andrew J. Mouland, PhD
Department of Medicine, Microbiology & Immunology,
Division of Infectious Disease
Lady Davis Institute

Project description:

Molecular and Cellular Biology of Pandemic Viruses – Ongoing projects include the structure function analyses of membraneless compartments also know an membraneless organelles generated by virus-mediated phase transitions in infected cells. We study pandemic HIV-1, SARS-CoV-2 and Influenza virus replication with the use biochemical, virological and super-resolution microscopy techniques. Students will be trained by experienced personnel and students and participate in cutting-edge research on pandemic viruses. The student will gain experience in manipulations in higher level biocontainment facilities and in several in vitro and in vivo assays in a highly collaborative and friendly atmosphere.

For more information:

https://www.ladydavis.ca/en/andrewmouland

https://www.mcgill.ca/expmed/dr-andrew-j-mouland

Pharmacology and Therapeutics

Using biosensors in primary cells and iPSC-derived organoid to study cellular signalling events

Supervisor: Terry Hébert, PhD
Department of Pharmacology
McGill Regenerative Medicine Network

Project description:

Recently, we have been able to quantify signalling *in cellulo*, using assays based on bioluminescence and Förster resonance energy transfer (BRET and FRET, respectively). We now generate signalling profiles in the single cell environment using high content microscopy (Jones-Tabah, J., et al (2021) https://pubmed.ncbi.nlm.nih.gov/34503973/), making it possible to compare the effects of potential therapeutic drugs in cultured heterologous cells with cells derived from patients. This project will expose students to the development and testing of FRET-based biosensors in cardiac organoids derived from patients with dilated cardiomyopathy.

For more information:

http://www.medicine.mcgill.ca/pharma/hebertlab/

Establishing an activity assay for the rhomboid protease RHBDL4

Supervisor: Lisa Munter, PhD
Department of Pharmacology & Therapeutics
Cell Information Systems Group

Project description:

The rhomboid protease RHBDL4 is an interesting protease since it is conserved during evolution suggesting that it carries fundamentally important functions. RHBDL4 localizes in the endoplasmic reticulum and appears to be involved in the regulation of protein and membrane transport. Clinically, high RHBDL4 expression associates with cancer. Our lab found that one of the substrates of RHBDL4 is the amyloid precursor protein (APP) that is causatively linked to Alzheimer's disease. We want to better understand under which cellular conditions RHBDL4 gains and loses activity. To this end, we have begun to develop several RHBDL4 activity assays. This summer project will include a) getting comfortable in the lab (1-2 weeks), validation of one assay (2-3 weeks), and exposing cells to different cellular stimuli and measure the effects on RHBDL4 activity (most of the time). You will use cell culture, transfection, RHBDL4 activity assays either fluorescent or luminescent, and western blots.

For more information:

http://www.munterlab.com/

Physiology

Nanomedicine for cystic fibrosis therapeutics

Supervisor: John Hanrahan, PhD
Department of Physiology
Cystic Fibrosis Translational Research Centre

Project description:

This project is to characterize newly developed nanocarriers for therapeutics to treat cystic fibrosis (CF). Airway epithelial cells will be exposed to polymeric nanoparticles loaded with CF drugs and/or anti-inflammatory compounds and examined for rescue of CFTR function (the defective protein in CF) using electrophysiology and inflammation using qPCR. The experiments will test the hypothesis that slow, sustained delivery of these compounds from nanocarriers is more effective than bolus exposure using a conventional vehicle.

For more information:

https://www.mcgill.ca/cftrc/

https://www.mcgill.ca/cftrfunction/

https://www.mcgill.ca/physiology/directory/core-faculty/john-hanrahan

Killing cancer and senescent cells with new designer nanoparticles

Supervisor: Ursula Stochaj, PhD
Department of Physiology
Quantitative Life Sciences

Project description:

Our laboratory is particularly interested in the impact of stress, metabolism, or aging on human health. All of these factors make significant contributions to the onset and progression of some of the most debilitating diseases. This includes cancer, type 2 diabetes, and aging-associated organ failure. Our group investigates these problems with modern methods in physiology, cell biology and biochemistry. The current project is an innovative approach that is relevant to the health of numerous individuals world-wide. Specifically, we will explore novel avenues to kill cancer and senescent cells. The project will provide the student with a diverse set of skills relevant to research in the medical sciences.

For more information:

https://www.mcgill.ca/physiology/directory/core-faculty/ursula-stochaj

https://www.mcgill.ca/qls/researchers/ursula-stochaj

Investigating the immune phenotype of vitamin D deficient mice

Supervisor: John White, PhD
Chair, Department of Physiology

Project description:

Vitamin D deficiency infants and children is linked to increased risk of autoimmune diseases, such as type 1 diabetes, later in life. This strongly suggests that vitamin D controls a process known as negative T cell selection that takes place in the thymus and eliminates self-reactive T cells. We have found that thymic development in mice that cannot make the active form of vitamin D is impaired – thymi are substantially smaller and thymic cell differentiation is disrupted in the absence of active vitamin D. Production of a key transcription factor necessary for the negative selection process is also inhibited. Moreover, mice display the hallmarks of autoimmune attack of peripheral organs, including insulin-producing pancreatic islets, later in life. The goals of the project are to understand how vitamin D signaling controls thymic development and the key gene transcription events necessary for negative T cell selection.

For more information:

https://www.mcgill.ca/vitamindlab/

Lady Davis Institute

Deciphering the role of integrated stress response (ISR) in lung cancer

Supervisor: Antonis Koromilas, PhD.
Lady Davis Institute for Medical Research
Gerald Bronfman Department of Oncology
McGill Regenerative Medicine

Project description:

Lung cancer is the leading cause of cancer death in men and women worldwide. Non-small cell lung cancer (NSCLC) constitutes 80% of all lung malignancies with 15-25% of NSCLC cases attributed to mutations in KRAS gene.

An important mechanism of cancer formation is the adaptation of cells to oncogenic forms of stress. This process involves the phosphorylation of the translation initiation factor eIF2 (p-eIF2α), which is a master regulator of translational and transcriptional reprogramming known as the integrated stress response (ISR).

My lab employs genetic, biochemical, and biological approaches to demonstrate the tumorigenic function of ISR in mouse and human models of mutant KRAS cancer (Nature Communications 2021). Our further goals are to decipher the oncogenic pathways regulated by ISR in lung tumor development, their crosstalk with immune regulatory pathways in tumor bed, and ISR implications in lung cancer treatment with a new generation of mutant KRAS drug inhibitors.

For more information:

https://www.ladydavis.ca/en/antoniskoromilas

Inhibiting arginine methylation to enhance immunotherapy

Supervisor: Dr. Stéphane Richard
Lady Davis Institute for Medical Research
Department of Oncology
Department of Medicine, Division of Experimental Medicine
McGill Centre for Translational Research in Cancer

Project description:

Arginine methylation plays an essential role in regulating inflammation, immunity, and antiviral responses, in particular, by methylating RNA binding proteins and regulating RNA splicing and epigenetics. Although more detailed analyses are required, multiple studies propose that PRMTs can be targeted to improve inflammatory-related diseases, as well as leukemias and lymphomas. The development of drugs targeting the activity of PRMTs has gained significant momentum in the last several years, and the inclusion of PRMT inhibitors in current clinical trials warrants continued research on arginine methylation. The prospect of using PRMT inhibitors to enhance immunotherapy is gaining momentum. The summer project would be to define the mechanisms by which inhibition of PRMTs leads to increase interferon signaling and regulation of the PD-L1/PD-1 axis in immunotherapy.

For more information:

https://www.ladydavis.ca/en/stephanerichard

Characterization of glioma-inhibitory macrophages

Supervisor: Donna L. Senger, PhD
Lady Davis Institute for Medical Research
Gerald Bronfman Department of Oncology
Department of Anatomy and Cell Biology
Department of Medicine, Division of Experimental Medicine

Project description:

Glioblastoma is the most lethal form of primary brain cancer. Current therapeutic approaches have focused almost entirely on the cancer cells. Although this strategy has led to a better understanding of the disease, advances in the clinic remain disappointing with survival rates still measured in months. While there are a large number of potential contributing factors, we believe the cells within the host organ where the tumor resides, influences the establishment, growth, progression, and therapeutic resistance of these tumors. We propose that the unique interaction that occurs between the tumor cells and the surrounding normal brain cells is a major contributor to the clinical challenges of treating this disease. We further propose that specific immune cells within the tumor environment, called macrophages, can be instructed to attack the tumor cells, and provide durable therapeutic response**.** We recently discovered a unique subpopulation of macrophages in brain tumors with glioma inhibitory abilities that result in long-term survival. In this project we will focus on the molecular and phenotypic characterization of these glioma inhibitory macrophages both *in vitro* and *in vivo*.

For more information:

https://www.ladydavis.ca/en/donnasenger

https://www.mcgill.ca/oncology/donna-senger

Research Institute – McGill University Health Centre (RI-MUHC)

Effects of phytocannabinoids on Natural Killer (NK) cell-mediated killing of breast cancer cells

Supervisor: Dr Cecilia Costiniuk
RI-MUHC
Department of Microbiology and Immunology
Department of Experimental Medicine
IDIGH Program

Project description:

Studies have shown that phytocannabinoids exert anti-tumor effects. However, relatively little is known about their effects on the tumor microenvironment, which is infiltrated by various immune cells including NK cells. The latter kill cancer cells without prior sensitization and MHC-restriction. They express a multitude of activating and inhibitory receptors, which bind with their cognate ligands expressed on the surface of cancer cells. NK cell-mediated killing depends upon the expression of these receptors on NK cells as well as of their cognate ligands on the surface of cancer cells. The student will investigate how cannabinoids (CBD and THC) modulate the expression of NK cell receptors and their cognate ligands on the surface of cancer cells, and modulate killing. The studies will be conducted in vitro using human breast cancer cell lines and NK cells from healthy individuals. The methodology will include cytotoxicity assays, flow cytometry and real-time RT-PCR.

For more information:

https://rimuhc.ca/-/cecilia-costiniuk-md-msc

Developing a bioinformatics pipeline for genomic analysis

Supervisor: Alex Gregorieff, PhD
RI-MUHC
Rosalind and Morris Goodman Cancer Research Centre
McGill Regenerative Medicine Network
Department of Pathology

Project description:

The intestinal stem cell (ISC) field has grown immensely over the last decade revealing key signals driving the self-renewing capacity of the gut epithelium and how dysregulation of these signals promotes tumorigenesis. However, recently it has become clear that the characteristics of adult ISCs are not fixed but are highly dependent on their environment. Through the study of injury or infectious models, we and others have found that the gut epithelium gives rise to distinct stem cells that transiently adopt features of the embryonic gut epithelium to replenish homeostatic pools of ISCs. This process, termed fetal reprogramming, has also been implicated in colorectal cancer as a response mechanism to anti-cancer therapy. In order to further investigate the basic processes driving cellular plasticity in tumor cells, the major objective of the summer project will to develop and characterize CRISPR-based models of murine colorectal cancer organoids.

For more information:

https://rimuhc.ca/-/alex-gregorieff-phd