We have just launched the 2025 Jacobo and Estela Klip Award to support Latin American, Spanish and Portuguese graduate students and postdoctoral fellows interested in collaborative research with one of the laboratories of the Cell Biology Program of the Hospital for Sick Children (SickKids) in Toronto, Canada.

The Jacobo and Estela Klip Fund will provide \$15,000 (CAD) to support the travel and accommodation expenses for successful candidates to spend a period of 4-6 months in a laboratory of their choice in the Cell Biology Program at SickKids.

We encourage you to share this opportunity with your graduate students and postdoctoral fellows.

- How to apply: <u>https://sickkids.slideroom.com/#/login/program/77797</u>
- List of eligible supervisors and research topics: <u>https://docs.google.com/document/d/16RhXSNdZVvzqgRLGeCGETAe</u> <u>zHr04UgFmnkMy9lhNPvc/edit?usp=sharing</u>



# Cell Biology Supervisors

Researchers in the Cell Biology program use cutting-edge methods in cell and molecular biology, biochemistry, and microscopy, combined with proteomics, combinatorial chemistry and high-throughput robotics. Our research examines cell physiology, inter and intracellular signalling, cell structure, and organelle function, on both a cellular and molecular level. We use cell models both in culture and in vivo to model disease states and define normal mechanisms.



Title: Senior Scientist, Cell Biology

Designations: MD, PhD, FRCPC

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**U of T Positions:** Professor, Departments of Paediatrics and Biochemistry and the Institute of Medical Sciences

Chair Positions: Canada Research Chair (Tier 1) in Paediatric Inflammatory Bowel Disease

Website: https://www.sickkids.ca/en/staff/m/aleixo-muise/

#### Research

Dr. Muise's research lab conducts translational research to identify and understand the causes of very early onset intestinal disease in children. His research has made it possible for many young children from across Canada and internationally to receive appropriate, personalized treatment, including nutritional therapy and stem cell transplant. These discoveries have already had a major impact on the clinical care of many patients and will fundamentally change the way that children are treated with both rare and common forms of intestinal disease.

The Muise Lab routinely performs whole exome sequencing (WES) or whole genome sequencing (WGS) to screen young children with intestinal disease for known and novel genetic variants. Results are then analyzed using a searchable database to enable rapid understanding of causal, risk, modifying, and treatment specific genes associated with these diseases. In addition to identifying genetic causes for novel diseases, state-of-art technology such as human intestinal organoids ("mini guts"), animal models (mouse and zebrafish), and functional assays are used to further define molecular variants. High-throughput screening (HTS) is also used to search for existing and new therapies that may target a specific gene or pathway.

Muise partners with numerous clinicians and researchers worldwide to identify additional rare disease patients, accelerate research and disease modelling, and promote advanced academic training. This has led to large scale funding and industry partnerships that make his lab an international leader in the study of paediatric gastrointestinal diseases.



Title: Scientist, Neurosciences and Mental Health

Designations: PhD, B.Sc.

Website: https://www.sickkids.ca/en/staff/s/amra-saric/

#### Research

The Saric Lab studies membrane trafficking - the process by which sub-cellular compartments called organelles are generated, remodeled and transported to support metabolism. They employ cutting-edge approaches in advanced microscopy, molecular biology and biochemistry to gain insight into how mutations affecting membrane trafficking lead to disease, particularly of the nervous system. Projects are currently focused on inter-organelle crosstalk and membrane contact sites, autophagy and tubular lysosome biogenesis.



Title: Associate Chair of Research, Department of Paediatrics

**Designations:** MD, PhD, FRCP(C)

U of T Positions: Professor, Department of Paediatrics

Chair Positions: Canada Research Chair, Rare Childhood Brain Tumours

Website: https://www.sickkids.ca/en/staff/h/annie-huang/

#### Research

Dr. Huang started the <u>Rare Brain Tumour Consortium</u> to pursue her long-standing research and clinical interest in rare infant brain tumours due to the distinct clinical challenges of these patient population. In her laboratory she combines genomics, functional epigenomics and genome-wide screening tools to understand the pathogenesis of rare CNS embryonal tumours, including ATRTs (Atypical Teratoid Rhabdoid tumours), and ETMRs (Embryonal Tumour with Multi-layered Rosettes) with the goal to improve treatment and patient survival. Many of the discoveries from the Huang lab has been applied to analyses and development of clinical trials for rare tumours through her leadership in the Children's Oncology Group Trial Consortia. Due to her specific clinical and research interest/expertise, she also frequently advises on treatment of children across the world diagnosed with rare CNS tumours.



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#### Research

Dr. Sayed is an Associate Scientist Track with a background in cellular immunology. His research is focused on understanding the molecular machinery controlling the development of allo-immunity following solid organ transplantation. This includes an interest in the epigenetic mechanisms of memory formation in cells of both the adaptive and innate immune systems. Dr. Sayed is a member of the Cell Biology program and his mentor is Dr. Sergio Grinstein.

#### SickKids RESEARCH INSTITUTE Benjamin Steinberg

**Title:** Staff Anesthesiologist, Department of Anesthesia and Pain Medicine/Cell Biology

Designations: MD, PhD, FRCPC

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U of T Positions: Assistant Professor, Department of Physiology

#### Research

The Steinberg Lab investigates fundamental interactions between the nervous system and immune system. This work aims to better understand how the body's nervous system monitors and controls inflammation. Direct cellular communication between neurons and immune cells allows the nervous system to modify how the immune system behaves in diseases such as sepsis, pain, and heart failure.

A better understanding of the interaction between the nervous and immune systems can help start to build therapeutics that target the nervous system to diagnose and treat inflammation-driven illnesses. This bioelectronic approach has the potential to impact on a variety of clinically important diseases in both adult and pediatric populations.



# **Christoph Licht**

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Website: https://www.sickkids.ca/en/staff/l/christoph-licht/

## Research

Dr. Licht's research has translational character and is focused on complement-mediated renal diseases, i.e. atypical haemolytic-uremic syndrome (aHUS) and membranoproliferative glomerulonephritis (MPGN)/C3 Glomerulopathy (C3G). Besides exploring new complement-targeting treatments, his team investigates the cellular and molecular consequences of complement activation on endothelial and epithelial cells and their interactions with platelets and neutrophils.

They recently became interested in the presence and function of intracellular complement, in particular in skeletal muscle. The team investigates the role of complement in the pathogenesis of an expanding spectrum of complement-mediated diseases, including sickle cell disease, acute/chronic injury of neuronal tissue, and chronic proteinuric kidney disease. Most recently, they began investigating the role of complement in COVID-19 pathology, in particular the related injury of the vascular endothelium.



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## Research

Brain tumors are the largest group of solid tumours and the leading cause of cancer-related death in childhood. The most devastating are paediatric high-grade astrocytoma (pHGA), including diffuse intrinsic pontine glioma (DIPG). These are incurable tumours with a median survival under two years. They respond poorly to conventional therapy and drug trials based on adult HGAs have not succeeded.

The discovery of recurrent histone mutations (H3K27M and H3.3G34R) in pHGA by us and others provided important clues regarding the role of epigenetic in the pathogenesis of these cancers. But despite these important genetic findings, there is still no effective treatment for these children.

The Hawkins lab is particularly interested in understanding what drives these tumours and how we can use this information to develop new therapies.



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## Research

The Rotin group has been studying the ubiquitin system, particularly the Nedd4 family of E3 ubiquitin ligases. They are studying the biochemistry, structure and function of these E3 ligases, as well as their physiological functions using cells, tissue organoids and model organisms.

They have developed proteomic methodologies to globally identify substrates for E3 ubiquitin ligases, and have subsequently focused their studies on some of the membrane proteins that were identified in these and related screens (e.g. the sodium channel ENaC, the FGF receptor 1, LAPTM proteins). These studies are relevant to human diseases such as hypertension, cystic fibrosis and cancer.



## James Rutka Title: Neurosurgeon, Division of Neurosurgery Designations: MD, PhD, FRCSC, FACS, FAANS

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U of T Positions: RS McLaughlin Professor and Chair, Department of Surgery

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## Research

Dr. Rutka's laboratory has been studying the cytoskeleton as a means to increase our understanding of the mechanisms by which astrocytoma cells grow, adhere to surrounding tissues, and invade normal brain tissue. Many cytoskeleton related genes and proteins are mutated in cancer and current studies are aimed at investigating the Rho-GTPase pathway for potential targets to inhibit astrocytoma invasiveness.

The Rutka lab is actively exploring the application of novel technologies for tumour therapies including delivery of therapeutics to the tumour using gold nanoparticles and temporary disruption of the blood-brain barrier with focused ultrasound to facilitate drug entry into the tumour while avoiding damage to normal brain tissues. Dr. Rutka's lab is interested in developing new strategies of drug delivery to metastatic medulloblastoma and patients with diffuse intrinsic pontine glioma and is adapting ultrasound technology to precisely target the tumours, open the blood-brain barrier to permit drug access and deliver novel drug compounds attached to gold nanoparticles.



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## Research

The goal of Dr. McGlade's research program is to understand the specificity and dynamics of protein-protein interactions involved in cell signaling and the molecular basis of signaling events that can be targeted in cancer. Towards this goal, her team focuses on the molecular structure, cellular functions and interaction networks of modular adaptor proteins that regulate critical oncogenic signaling pathways. Currently, the lab is using structural, proteomics, and genetic screening approaches to identify protein networks and specific targets involved in tyrosine kinase signalling and alternative splicing in cancer, as well as high-throughput assays to identify small molecule regulators of ubiquitin ligases.



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## Research

Dr. Youn joined the SickKids Research Institute to establish her lab in June 2020. Her lab studies biomolecular condensates that organize subcellular systems and govern their ability to deal with stress. Using proteomics, genomics, and cell biological tools, her team investigates their organization, dynamics, and function. This work provides novel strategies to understand and treat neurodegenerative disorders, cancer and infectious diseases.



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#### Research

Dr. Brumell's research examines the host-pathogen interface and employs genetic and cell biological approaches to understand these infections and their outcomes. This research focuses primarily on Salmonella and Listeria, which are common pathogens and powerful model organisms for the study of infection. In addition to this basic research, Dr. Brumell's lab also examines how host-pathogen interactions can impact the development of chronic diseases such as Inflammatory Bowel Disease and Arthritis.



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#### Research

Liquid-liquid phase separation has emerged as an key mechanism that regulates cellular organization. Biomolecular condensates, or 'membrane-less organelles', concentrate specific proteins, nucleic acids, and small molecules without an encapsulating membrane. The Ditlev Lab studies the role of liquid-liquid phase separation in organizing neuronal and immunological signaling pathways at the membrane of the cell. Ditlev's team uses a combination of biochemical reconstitution and cell biology to understand how the composition of biomolecular condensates dictates the function of the condensate. They are specifically interested in understanding the role that biomolecular condensates play in local actin polymerization, ion flux through membranes, and local RNA translation as well as understanding how the intrinsic biophysical properties of condensates determine the ability of condensates to associate with or repel other condensates on membranes.



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## Research

Phosphatidylinositol phosphates (PIPs) are membrane lipids with roles in cell growth, signaling and morphogenesis. Alterations in the levels of PIPs are associated with human developmental disorders and diseases such as cancers, yet little is known about the normal roles of PIPs during animal development.

The Brill lab investigates the roles of PIPs using powerful molecular genetic approaches available in the fruit fly *Drosophila melanogaster*. They have uncovered novel roles for PIPs and PIP pathway enzymes in sperm development, secretory granule maturation and tissue integrity. Brill's current research seeks to determine how PIPs and PIP pathway enzymes control these processes and to identify upstream regulators and downstream targets of PIP signaling.

In a second area of research, the Brill lab has recently begun to study mechanisms of post-transcriptional regulation and roles of long noncoding RNAs in sperm development. Because PIPs and RNA regulation play crucial roles in all eukaryotes, their results will reveal conserved cellular mechanisms that are fundamental to human development and disease.



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**Chair Positions:** Canada Research Chair (CRC) Tier 1 in Vascular Inflammation and Kidney Injury

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## Research

Robinson's research actively explores the mechanisms by which the immune system contributes to progressive kidney disease and to cardiovascular disease. Her research program integrates molecular biology, cell biology, advanced microscopic, and biochemical approaches with experimental models of inflammation, cardiovascular disease, and kidney injury.

Robinson's collaborative research program also explores new methods to optimize preservation of donor kidneys prior to transplantation.

As a clinician-scientist and paediatric nephrologist, Robinson's ultimate goal is to use the new knowledge generated from her research to transform the care that children with kidney disease receive. Understanding the pathogenesis and complex biology that underlies inflammatory renal disease is critical for the design of innovative, rational therapies.



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#### Research

After finishing his medical training at McGill University and the University of Toronto, Dr. Lemaire did a PhD in Investigative Medicine focused on the genetics of rare paediatric kidney diseases. Work in his lab is currently focused on understanding the pathophysiology of novel forms of atypical hemolytic-uremic syndrome (aHUS) that his group discovered using exome sequencing. One project relates to diacylglycerol kinase epsilon (DGKE) nephropathy and phosphoinositide signaling in endothelial cells. Other projects are focused on studying the function of other genes associated with novel forms of aHUS. Meanwhile, he continues to perform gene discovery studies applied to pediatric patients with a variety of unusual renal phenotypes.



Title: Paediatrician-in-Chief, Department of Paediatrics

**Designations: MD** 

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#### Research

Irwin's laboratory research focuses on understanding the molecular determinants of neuroblastoma to identify novel therapies that target signaling pathways using a variety of cellular and animal models. Their translational research program is linked with the SickKids Kids Cancer Sequencing (KiCS) Program and national precision oncology for young people (PROFYLE) programs, with a focus on modeling novel germline and somatic variants. Irwin's research has been funded by Canadian Institutes of Health Research (CIHR), Canadian Cancer Society Research Institute (CCSRI), National Cancer Institute (NCI) and many neuroblastoma-focused foundations.

In addition to laboratory-based research she is involved in international efforts to develop risk classification systems and clinical trials for newly diagnosed and relapsed neuroblastoma. Locally, Irwin established the Neuroblastoma Program that is co-led by <u>Dr. Daniel Morgenstern</u> and includes a multidisciplinary team with expertise in the care of neuroblastoma patients. The program cares for local patients as well as provides expert consultations and access to local and international clinical trials and MIBG therapy.

As well as translational neuroblastoma research, Irwin is involved in the development of clinician-scientist training and education programs including the first residency research stream in Paediatrics in Canada. She also co-leads the SickKids ENACT committee which provides guidance for and access to innovative research testing and return of results.

- Role of p53 family genes in cancer and chemotherapy sensitivity
- Novel pathways and targeted therapies for neuroblastoma
- Molecular and genetic determinants of metastasis in neuroblastoma
- Genetic predisposition to Neuroblastoma
- Prognostic factors and Risk Stratification for Neuroblastoma
- Precision medicine



Title: Scientific Director, SPARC BioCentre

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U of T Positions: Professor, Department of Molecular Genetics

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## Research

Dr. Moran's research focus, publications, and invited seminars have addressed the intracellular signaling networks that control growth, survival, and spreading of tumours, and how drugs may be designed to target key components in these molecular networks. His group uses proteomics technologies including mass spectrometry and bioinformatics to identify and characterize proteins activated in cancers, and to determine drug mechanisms of action.



Title: Scientist, Cell Biology

Designations: PhD

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## Research

Neurodegenerative diseases, including Parkinson's, Alzheimer's and ALS, affect millions of people worldwide. Our current understanding of these conditions suggests the etiological basis of neurodegeneration involves the complex cross talk between genetic mutations, environmental factors, neuroinflammation and multiple cell types in the brain and periphery.

Interestingly, many disease-causing alleles, especially those affecting endocytic function, have direct deleterious effects on phagocyte populations in the brain and periphery. These cell types, microglia and macrophages, respectively, depend on intracellular trafficking pathways for their immune and homeostatic functions. Although previously underappreciated, the endocytic dysfunction of phagocytes in neurodegenerative disease likely contributes to the inflammation observed in the brain and periphery during neurodegeneration. Whether this is a direct consequence of trafficking defects on the phagocyte or an alteration in phagocyte interactions with neighboring cells or the microbiome/mycobiome, remain to be determined.

The Maxson laboratory focuses the study of (1) microglial and macrophage endocytic mechanisms that contribute to neurodegenerative disease, and (2) the putative role of fungal dysbiosis on neuroinflammation and neurodegeneration. The use of genetically tractable in vitro, iPSC, and in vivo disease models to study the interactions between cells in neurodegenerative diseases like Parkinson's, allow us to leverage state-of-the-art 4D high resolution imaging with robust quantitation methods to strengthen the connection between phagocyte endosomal pathways and neuronal health.



Title: Staff Anesthesiologist, Department of Anesthesia and Pain Medicine

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## Research

The Goldenberg laboratory studies immune dysfunction in the lung vasculature, focusing primarily on pulmonary arterial hypertension. The lab uses cell culture, animal models, and patient-derived samples to study the importance of the immune system in the development of this disease, with an eye toward designing new treatments for this devastating condition. To this end, they focus our studies on cell death, inflammation, and the role of endothelial cells and vascular smooth muscle cells in the development of pulmonary hypertension.



Title: Senior Scientist, Cell Biology

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#### Research

As a clinician scientist and paediatric gastroenterologist, her research focuses on understanding the mechanisms responsible for gastrointestinal inflammatory diseases including Helicobacter pylori and inflammatory bowel disease. She is passionate about supporting and developing the careers of clinician scientists through various roles including her role as Director of the Integrated Physician Scientist Training Program at the University of Toronto and previously as the principal investigator for the Canadian Child Health Clinician Scientist Program.



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#### Research

The human cell contains small compartments called organelles. Each organelle carries out specialized activities such as producing energy to breaking down toxins that are essential for the proper function of the cell.

Dr. Kim focuses on understanding how the cell maintains the numbers and functions of organelles. The primary focus of his research is to understand how two metabolic organelles, Peroxisomes and Mitochondria that makings and breakings down fats, are maintained by the cell.

Using high and super-resolution microscopy combined with genetic tools, Dr. Kim's laboratory is studying the mechanisms that control these two organelles and how defects in these mechanisms lead to various diseases from genetic disorders to severe malnutrition.



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#### Research

The Yeung Lab is seeking to understand the molecular and cellular mechanisms governing autoimmunity.

The central theme of my research program is to understand the molecular and cellular mechanisms governing autoimmunity towards discovery of molecular tools for improved disease diagnosis, treatment, outcomes and prevention – the foundations for precision medicine. Specifically, I study the mechanisms responsible for initiating and sustaining the immune response in autoimmunity with a focus on rare diseases of childhood – Kawasaki Disease, Systemic Vasculitis and Juvenile Idiopathic Arthritis.



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#### Research

Research in Dr. Kafri's lab is primarily aimed at introducing the question of size uniformity into the subject of cell size. Two fundamental questions are:

- 1. How do a common set of signals (including mTORC1) specify a different and distinct size for each of the different animal cell types?
- 2. When considering cells of a given type, how are numerous individual cells in the tissue regulated to have the same exact size? Paradoxically, Dr. Kafri's research findings on cell size have paved the road to a fundamentally new perspective on cancer prevention and cancer risk. Specifically, he examines whether a person's cancer risk derives from changes in the setpoint of mTORC1 homeostasis.



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#### Research

The Egan Lab has worked on Notch signaling in the mammary gland and breast cancer as well as on genetic screens to identify oncogenic mutations responsible for mammary tumor formation and metastasis.

The lab develops immune competent mouse models for mammary cancer as a means to probe genetic mechanisms responsible for tumor progression and metastasis, and also as a platform for the development of rational combination therapy which includes an immune-therapy component.

Models have been developed for a number of common genetic alterations associated with human breast cancer including commonly mutated genes such as PIK3CA, as well as chromosome arm losses. More recently, these models are being used to define oncogene-specific networks of mutations that promote tumor progression and metastasis.



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## Research

The Freeman Lab is working to understand cellular and mechanisms underlying immune surveillance. The immune system protects us from infection, orchestrates wound healing, and eliminates cancer. Such versatility necessitates detectors that distinguish harmful from healthy components as well as the ongoing sampling/turnover of tissues (i.e. surveillance).

In disease, immune surveillance is evaded by pathogens and tumor cells such that its protective role is lost. By using state-of-the-art, multidisciplinary approaches, the Freeman Lab is uncovering mechanisms of immune surveillance from single molecules to cells to populations.



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#### Research

Dr. Kahr's research is aimed at understanding the development and function of platelets, tiny blood cells that initiate and co-ordinate clotting at wounds. Platelets do this by adhering, aggregating and secreting a wide assortment of molecules, which helps normal clotting and can also contribute to thrombi that cause heart attacks and strokes. Many of his insights into the mechanisms of platelet development and function have come from studies of patients with inherited disorders. His particular interest is alpha granules, which platelets use to transport and secrete several hundred different proteins. His team has identified several proteins and cellular pathways involved in the development of alpha granules in the cells that produce platelets, the bone marrow megakaryocytes.