CBR-SBME RESEARCH DAY 2021

WEDNESDAY AUGUST 11, 2021

CBR
THE CENTRE FOR BLOOD RESEARCH

SBME UBC
SCHOOL OF BIOMEDICAL ENGINEERING

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Welcome to the virtual 2021 CBR-SBME Research Day.

Held annually to celebrate the conclusion of the Centre for Blood Research-School of Biomedical Engineering (CBR-SBME) Summer Studentship Program, this event showcases cutting-edge and innovative research projects conducted by undergraduate and medical students over the summer months.

This marks our second time hosting this event and Program virtually. Although the COVID-19 pandemic has presented many challenges and changes, we creatively adapted to a virtual format and continued to offer meaningful opportunities for summer students. We hope to bring back more in-person activities next summer, and are also excited to incorporate what we have learned during this unprecedented time into our future programming, bringing the best of two worlds together. Indeed, we are especially looking forward to the lively atmosphere that accompanies an in-person Research Day — as well as the much-loved BBQ!

Over the last few months, the summer students have not only honed their scientific skills, but have also expanded their professional horizons and networks through various career development workshops, socials, and skill development sessions. Event highlights include the Design Your Life workshop, Career Exploration Panel, Lay Summary Writing and Presentation practical skills sessions, and Escape Room and Paint Night socials. We hope these events, combined with hands-on research, have provided a well-rounded summer experience.

Established in 2011 by the CBR, this long-standing Summer Studentship Program has grown tremendously from its initial cohort of 13 students. Since 2019, the CBR and SBME have successfully partnered together to expand the program's offerings and bring more research opportunities to students. We were proud to support 31 CBR-SBME summer students with funding this year, and we look forward to the Program's continued growth in the future.

To this year's summer student cohort: we are so proud of all that you have accomplished! We hope you had an enjoyable experience as part of the CBR-SBME Summer Studentship Program, and we can't wait to see where your journey takes you next.

All the best,
Drs. Stefanie Mak and Carmen de Hoog
CBR-SBME Summer Studentship Program Managers

PROGRAM SCHEDULE

WEDNESDAY AUG. 11 | 10:00AM - 2:30PM PT

10:00 AM - 10:50 AM	**Welcome & Opening Remarks** **Keynote Presentation: Dr. Jennifer Willet**
10:50 AM - 11:00 AM	**Break**
11:00 AM - 12:15 PM	**Session 1: Summer Student Presentations**
12:15 PM - 12:45 PM	**Break**
12:45 PM - 1:55 PM	**Session 2: Summer Student Presentations**
1:55 PM - 2:30 PM	**Neil Mackenzie Mentorship Excellence Award** **Summer Student Awards** **Closing Remarks**

"INCUBATOR Art Lab: Radical interdisciplinarity in the arts and sciences"

Keynote Speaker: Dr. Jennifer Willet

Dr. Jennifer Willet is a Canada Research Chair in Art, Science, and Ecology and a Professor in the School of Creative Arts at the University of Windsor, Canada. She is the Director of INCUBATOR Lab, an art/science research laboratory and studio in downtown Windsor. She is also an internationally successful artist and curator in the emerging field of bioart. Her work resides at the intersection of art and science, and explores notions of representation, the body, ecologies, and interspecies interrelations in the biotechnological field.

RESEARCH DAY PRESENTERS & LAY SUMMARIES

Name	Supervisor(s)	Project Title
Adan Moallemi	Dr. Dena Shahriari	Optical stimulation to induce nerve fiber regeneration following spinal cord injury
Adrian Marcuzzi	Dr. David Liu	Using AI to improve image-guided spinal procedures
Alexander Golab	Dr. Dena Shahriari	High-throughput thermal drawing tower for producing multi-material fibers
Alexandra Witt	Dr. Ed Pryzdial	Mutant clotting factor X: A safer clot buster?
Amanda Murphy	Dr. Calvin Kuo, Dr. Osman Ipsiroglu, Scout McWilliams, Nadia Beyzaei	Recommendations for patient collected video in automated movement behavior analysis
Ardin Sacayanan	Dr. Zachary Laksman, Dr. Leili Rohani	Electro-mechanical stimulation and functional characterization of engineered heart tissue
Arian Sadigpour	Dr. Narges Hadjesfandiari, Dr. Dana Devine	Investigation of Laser Optical Rotational Red Cell Analyzer (Lorrca) Indices in Donor Populations
Atishay Jay	Dr. Nancy Fang, Dr. Peter Zandstra	Automated Flow cell for *in-situ* Biomolecular Imaging
David Chen	Haisle Moon, Dr. Jayachandran Kizhakkedathu	Advancements Towards Universal Blood: Immuno-camouflage of Red Blood Cells
David Mackay	Priye Iworima, Dr. Tim Kieffer	Effect of mTeSR Plus on Pluripotent Stem Cell Growth
Elijah Martin Tongol	Arshdeep Gill, Dr. Jayachandran Kizhakkedathu	Iron Chelating Polymer Adjuvants for Treatment of Bacterial Biofilm
Emily Chan	Dr. Natalie Strynadka, Bronwyn Lyons	Shaping the vaccine against *Chlamydia trachomatis*
Emmanuel Garrovillas	Dr. Edward Conway	Elucidating the relationship between CD248 and PDGF in Type II Diabetes

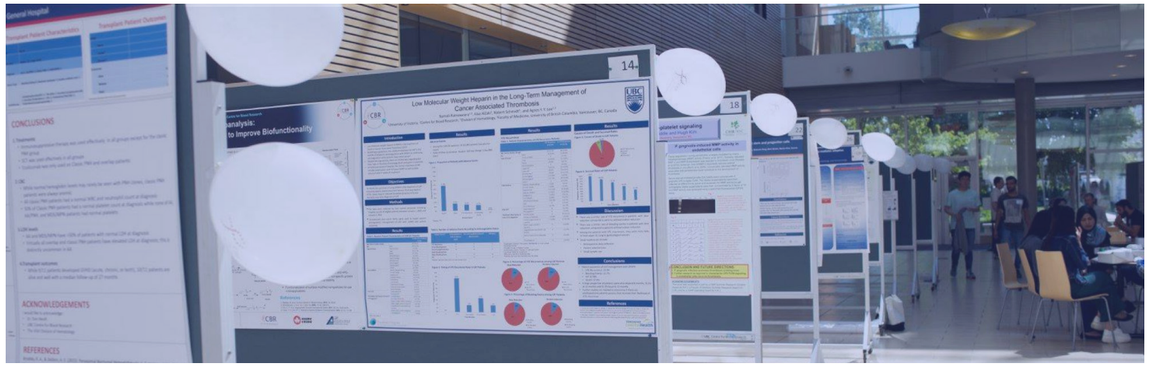
31 **summer students**
supported with CBR-SBME funding in 2021

11 years
of program growth, research excellence, & mentorship

40+ principal investigators & research teams
participating over the years

180+
students supported
since 2011

Name	Supervisor(s)	Project Title
Eric Lyall	Dr. Carolina Tropini	Using the eVOLVER automated cell culture platform to investigate phage-host dynamics and evolution during changes in osmolality
Francesca Ferraresso	Dr. Christian Kastrup	RNA Therapy for Thrombotic Disorders
Hailey Chapman	Dr. Hélène Côté	Mitochondrial DNA Mutations of Sorted Lymphocytes in People Living with HIV and Not
Han Nguyen	Dr. Lyndia Wu	Customizable Flexible 3D Printed EEG Cap and Electrodes
Hoanne Chan	Dr. Hugh Kim	Probing Signaling in Platelets during Endocytosis
James (Hyun Ku) Chae	Samantha Ji Soo Yoon	Validation of human islet calcium-regulated genes and subtype markers
Janella Schwab	Kieran Maheden, Dr. Nika Shakiba	Non-specific RNA cleavage of CRISPR-Cas13d in mammalian cells
Jennifer Jiang	Dr. Nozomu Yachie, Dr. Soh Ishiguro	Harnessing vertebrate V(D)J recombination to develop a new high-resolution cell lineage tracing technology
Jonathan Gui	Dr. Peter Zandstra, Dr. Daniel Aguilar-Hidalgo	Modelling and Control and Stem Cell Signalling Domains
Karen Hwang	Omar Bashth, Dr. Nika Shakiba	Clonal interactions between normal and abnormal human stem cells
Kira Tosefsky	Dr. Shernaz Bamji	Role of PRG-1 Palmitoylation in Synaptic Plasticity
Kisa Naqvi	Dr. Carolina Tropini, Dr. Jen Nguyen	Visualizing the spatial organization of gut bacteria
Lucas Rempel	Dr. Fabio Rossi, Dr. Marine Theret	TAK1 signaling in mesenchymal stem cells regulates the type 2 inflammatory response



Name	Supervisor(s)	Project Title
Lydia Li	Dr. Ivan Robert Nabi	Microscopic Examination of Transmembrane Protein Helps Predict Cystic Fibrosis Treatment Outcomes
Max Arsenault	Dr. Dena Shahriari	Promoting Nerve Fiber Growth After a Spinal Cord Injury
Myles Ng	Dr. Natalie Strynadka	Structural Determination and Analysis of SAR-CoV-2 M^{pro}
Nadine Truter	Dr. Dena Shahriari	Biomaterials-Based Scaffolds to Guide Axonal Growth After Spinal Cord Injury
Parvin Malhi	Dr. Andrew Shih, Dr. Krisztina Vasarhelyi, Dr. Maya Gislason	Exploring the Potential of Convalescent Plasma Therapy and Other Experimental Therapies as an Intervention in the Pandemic Response; CONCOR-1 as a case study
Puneet Sidhu	Dr. Jenna Usprech	Educating Scientists on Risk Communication in a Public Health Emergency
Quan Nguyen	Dr. Michael Hughes, Dr. Hugh Kim	The role of platelet factor 4 (PF4) in rheumatoid arthritis
Rehan Jessa	Dr. Alina S. Gerrie	Clinicopathologic characteristics and treatment outcomes of plasmablastic lymphoma in British Columbia
Ryan Hong	Dr. Kurt Haas	Characterizing functional impacts of ACE2 receptor variants on COVID-19 disease pathophysiology
Simranpreet Mann	Dr. Bhavjinder Dhillon, Dr. Robert E. Hancock	A Meta-Analysis of COVID-19 Disease Outcomes
Yasmine Lau	Dr. Michael Hughes, Dr. Kelly McNagny, Kristen Li	Chemically Induced Kidney Failure in Podocalyxin Heterozygous Mice

OPTICAL STIMULATION TO INDUCE NERVE FIBER REGENERATION FOLLOWING SPINAL CORD INJURY

Adan Moallemi
Supervisor(s)/Collaborator(s): Shahriar Shalileh, Dena Shahriari

The spinal cord is a crucial for facilitating our day-to-day activities. Damage to the spinal cord results in paralysis and organ dysfunction in areas of the body at and below the site of injury. Moreover, damaged nerve fibres in the spinal cord cannot spontaneously regenerate, thus an intervention is needed to induce regeneration in order to repair these damaged regions. Optogenetics is a technique in which cells can be genetically modified to respond to light by injecting a virus containing the genes of light-sensitive ion channels. While optogenetics has been widely used in neuroscience to understand brain circuitry and dysfunctions, its power has not been harnessed when it comes to the spinal cord, particularly when it comes to regeneration studies. The basis of this project is to sensitize nerve fibers in the spinal cord to light by injecting this virus. Why sensitize these fibres to light? Previous *in vitro* studies have found that optically stimulating nerve cells results in a significant amount of cell growth. We hope to take these findings and translate them to an *in vivo* model in hopes of observing the same growth in damaged nerve fibres. Before we get to that point, we must ensure that there are optimal levels of expression of these light-sensitive ion channels following virus injection. Following injection, we observed robust expression of this light-sensitive channel. With these findings, we can now proceed to regeneration and functional recovery studies.

USING AI TO IMPROVE IMAGE-GUIDED SPINAL PROCEDURES

Adrian Marcuzzi
Supervisor(s)/Collaborator(s): Jessica C. Küpper, Simon Alexander, Matthew Wiens, Rashmi Prakash, Adnan Sheikh, David Wilson, Paul Cooper, David Liu

There are several medical procedures that require interventional radiologists to take CT scans and find the appropriate location to operate on. This includes injections of pain medication, surgeries on the spine, and operations on vertebrae – the bones of the spine. It can be difficult to manually identify the vertebrae, and there have been cases of procedures being performed at the wrong vertebral level.

To mitigate this risk, a research team at the UBC Department of Radiology, the Centre for Hip Health and Mobility, and Libang Surgical Technologies Inc. is developing a machine learning algorithm to automatically identify the specific vertebrae and smaller anatomical features on a CT scan prior to procedures.

To train the algorithm, a preliminary dataset is being curated from 374 open access CT scans, which will supplement additional CT data currently being approved by the Institutional Review Board. The scans were reviewed, with exclusion of spines with scoliosis - lateral deviation of vertebrae – and metal inserts. This provided a total of 212 CT scans, which are currently in the process of having their vertebrae manually labeled. Labeled datasets like this are used to train machine learning algorithms in a process called “supervised learning”, where the algorithm compares its answer to a “ground truth” and iteratively adjusts its methods to be accurate.

In the upcoming months, the team will train models and develop an automated method to identify vertebrae and other features. Later, the AI will be used in a robotic arm being developed for needle-guided procedures.

HIGH-THROUGHPUT THERMAL DRAWING TOWER FOR PRODUCING MULTI-MATERIAL FIBERS

Alexander Golab
Supervisor(s)/Collaborator(s): Dena Shahriari, Shahriar Shalileh

Thermally drawn fibers are thin and flexible thread-like structures capable of being manufactured to tiny sizes. Through thermal drawing, a process in which we heat a finely made collection of material called a preform to its softening temperature in a furnace, then drawn out, we can create a variety of fibers. We can manufacture these fibers out of multiple materials, enabling them to have a variety of properties, such as electrical conductivity, or hollow channels, allowing for their use in neural probes, wearable electronics, etc. Although the knowledge of how to make these fibers isn't new, it is still difficult for laboratories to get a thermal drawing tower needed to make these fibers. The aim of my project has been to make an easily accessible thermal drawing tower allowing for the production of multi-material fibers. The tower aims to enable control over the fiber size by adjusting the preform feed rate, wire drawing rate, and the temperature of the furnace. If a laboratory wishes to follow the design, it would cost them $15,000-$20,000 to create one, far cheaper than the million dollars seen by commercial towers. I hope that this thermal drawing tower gives other laboratories the ability to create these multi-material fibers, enabling further studies.

MUTANT CLOTTING FACTOR X: A SAFER CLOT BUSTER?

Alexandra Witt
Supervisor: Ed Pryzdial

Strokes and heart attacks, caused by blood clots, are currently being treated by a clot busting drug with very serious side effects, such as brain bleeds. The Pryzdial lab has created a new drug by making changes to clotting factor X, a protein in your blood that normally helps form blood clots. With one mutation that inhibits its natural clotting effects, and another that keeps the drug stable in the blood, the new drug should be able to act as a clot busting cofactor that doesn't break down and lose its necessary clot busting activity. After a lengthy purification process, we compared our mutated factor X to the wild-type version found in our blood, and demonstrated that our new drug won't break down into inactive pieces. Then, we tested the mutated factor X against the wild-type factor X in a simulated blood clot, showing that the two mutations help our new drug to speed up the clot busting process. Next, we will test our new drug in mouse models with carotid artery blood clots, which will test not only its ability to bust those clots, but its safety as well. We're hoping to continue testing and improving our drug until we can use it to save millions of lives.

RECOMMENDATIONS FOR PATIENT COLLECTED VIDEO IN AUTOMATED MOVEMENT BEHAVIOR ANALYSIS

Amanda Murphy
Supervisor(s)/Collaborator(s): Calvin Kuo, Osman Ipsiroglu, Scout McWilliams, Nadia Beyzaei

As access to medicine has decreased with the COVID-19 pandemic there has been a need to formulate better use of technology to provide quality remote patient care.

Video is one of the more common technologies for remote care because the average person can take videos and remotely transmit them to health care providers for diagnosing patients, particularly those where behavioral observations are required, such as ADHD, restless leg syndrome, and autism spectrum disorder. However, because of how much video can easily be taken by patients the amount of time needed to be dedicated to watching video can be too costly on the part of health care professionals and there needs to be guidelines on how to take video in a way that is the most effective. In my project I will be analysing the robustness of an algorithm called HMovements which identifies the which parts of video is of interest and feature movement at different angles, heights, and distances. This robustness is being found by looking at how accurate HMovements is at identifying when movement occurs at these different heights, angles, and distances. These accuracies will be used for educating patients and others who may be taking video on the best practices for taking video for use in HMovements.

ELECTRO-MECHANICAL STIMULATION AND FUNCTIONAL CHARACTERIZATION OF ENGINEERED HEART TISSUE

Ardin Sacayanan
Supervisor(s)/Collaborator(s): Zachary Laksman, Leili Rohani, Mishal Ashraf, Kate Huang, Jeremy Parker, Jared Churko

Several studies have demonstrated the ability to produce engineered heart tissues from human stem cell. This model system has the capacity to reproduce patient specific genetic traits and has the potential to be used for systematic drug and disease screening. A critical factor for maturing tissues efficiently, and an important element of experimentation, is the ability to stimulate these tissues with electricity at constant voltage and frequency. However, most pulse generators on the market are quite expensive and can only produce a current in one direction which does not accurately replicate the environment of a heart cells which has current going forward and backwards. We have therefore set out to build, integrate and test our custom electrical stimulation capable of producing current in two directions into our optical mapping setup which consists of a custom microscope that is capable of recording voltage changes in the tissues using a high-speed, high-resolution camera and voltage-sensitive dye.

INVESTIGATION OF LASER OPTICAL ROTATIONAL RED CELL ANALYZER (LORRCA) INDICES IN DONOR POPULATIONS

Arian Sadigpour
Supervisor(s)/Collaborator(s): Narges Hadjesfandiari, Dana Devine

Red Blood Cells (RBCs) depend on their unique flexibility to fit through tight spaces — such as those found in one's smallest blood vessels — so they can deliver oxygen to tissues and keep them alive. Some people have RBCs that don't have the flexibility to function properly. These cells are broken down at a higher rate than in a healthy person, resulting in less than ideal blood transfusion outcomes. Understanding donor factors affecting RBC quality can help improve blood transfusion outcomes.

Laser Optical Rotational Red Cell Analyzer (Lorrca) measures how flexible RBCs are by observing their shape when subjected to differences in pressure or number of dissolved particles in a fluid. In this project, I demonstrate that long storage times result in reduced RBC flexibility; fatty environments increase RBC flexibility in males; sex does not affect RBC flexibility; water contents in RBCs increase as people age; and that Lorrca shows promise as a replacement to one of the Devine Lab's current methods of measuring RBC quality. My findings provide a reference range for Lorrca measurements. These measurements can be used as a baseline in future projects in the Devine Lab that ask why storage outcomes vary in different donors.

AUTOMATED FLOW CELL FOR *IN-SITU* BIOMOLECULAR IMAGING

Atishay Jay
Supervisor(s)/Collaborator(s): Nancy Fang, Peter Zandstra

Conventional gene expression profiling tools such as single-cell RNA sequencing allow quantitative measurement of gene expression change but fail to register the spatial context of this expression that arises from cell-cell interactions or other cues. Protocols such as Fluorescent *in-situ* sequencing (FISSEQ) help address this issue by preserving the native structural environment of cells and identifying spatially confined genetic elements involved with the regulation of gene expression. However, FISSEQ is a labor-intensive protocol demanding multiple rounds of sequencing chemistry steps in between image acquisition rounds on microscopes to preserve and process the spatial context of gene expression.

Therefore, my project at the Zandstra lab involved the construction of a fully automated fluid perfusion device called a flow cell capable of perfusing reagents through samples on coverslips at desired temperature unsupervised. The main goals of the project were to achieve precise and stable temperature and fluid control within the flow cell according to sequencing requirements, integrate in-house Python automation scripts with the flow cell, and process imaging data autonomously to generate sequences that highlight localized gene expression. So far, the performance of the flow cell controlled by automation scripts has been validated using Fluorescent *in-situ* Hybridization (FISH) experiments where human pluripotent stem cells (hPSCs) underwent gastrulation differentiation and had been fixed and stained together with undifferentiated hPSCs for pluripotency/ectoderm marker SOX2 for imaging. Next steps is to perform an automated run of FISSEQ on the validated flow cell while developing the autonomous image analysis pipeline to infer gene expression dynamics.

ADVANCEMENTS TOWARDS UNIVERSAL BLOOD: IMMUNO-CAMOUFLAGE OF RED BLOOD CELLS

David Chen
Supervisor(s)/Collaborator(s): Haisle Moon, Stephen Withers (Withers Group), Jayachandran Kizhakkedathu

Blood transfusion is a potentially life-saving procedure that can benefit patients who experience major blood loss during surgery, injury, or disease. However, blood transfusion requires matching of blood types to avoid serious complications. Both the matching of the A, B, and O types, as well as the matching of minor blood types are a requirement in clinical transfusions, as complications may also arise from mismatched blood types, which in some cases can be fatal. Here we aim to modify A type red blood cells to evade immune recognition. We utilized an enzyme pair that cleaved the characteristic A antigen of the A type red blood cell, converting these cells to the O type. To tackle the issue of minor blood type matching, we grafted a molecule called polyethylene glycol to the red blood cell surface to shield the minor blood antigens from recognition by the recipient immune system. Following incubation of these modified red blood cells in donor serum of various blood types, substantial decreases in immune recognition were observed compared to unmodified blood cells. These modified cells also demonstrated similar osmotic stability and functionality to unmodified red blood cells as well. The current results unveil strong potential for the modification of A type red blood cells into a universal blood product. We aim to further study the stability of these modified cells in donor serum and during long term storage.

EFFECT OF mTeSR PLUS ON PLURIPOTENT STEM CELL GROWTH

David Mackay
Supervisor(s)/Collaborator(s): Priye Iworima, Tim Kieffer

Pluripotent stem cells (PSCs) are able to make copies of themselves and become any other cell type in our bodies. Other cells made from PSCs can be used to replace defective or damaged cells in a patient's body, but producing enough cells to treat everyone is still a challenge. To overcome this challenge, we can design better environments to grow PSCs that can be used for downstream applications. Cells are grown in liquid media filled with nutrients. MTeSR1 is one of the most common media for growing PSCs, and is sold by STEMCELL Technologies. MTeSR1 was developed in 2007, but an improved version, mTeSR Plus, has been developed with a more stable growth factor. The effects of growing PSCs in mTeSR1 and mTeSR Plus were assessed. PSCs grown in mTeSR1 had their media replaced daily, while PSCs grown in mTeSR Plus had their media replaced every other day. Cell number, viability, and protein markers were measured for both sets of cells. The cells grown in mTeSR Plus had an improved growth rate and cell yield compared to the ones in mTeSR1, but both had similar viability and protein markers. An improved growth rate will give researchers more flexibility in feeding strategy, along with producing more cells using less resources (time, media, and cost). As we continue to improve the growth environment of PSCs, the closer we will be to developing treatments made from PSCs.

IRON CHELATING POLYMER ADJUVANTS FOR TREATMENT OF BACTERIAL BIOFILM

Elijah Martin Tongol
Supervisor(s)/Collaborator(s): Arshdeep Gill, Jayachandran Kizhakkedathu

Antibiotic resistance is a global phenomenon that threatens the effectiveness of antibiotics against infectious diseases. Certain bacteria are not easily eliminated by antibiotics because of their ability to cluster into a structure called biofilm. Despite using a higher dosage of antibiotics, these bacteria are not eliminated, leading to persistent infections. My project uses a chelator, a binding agent, that lowers iron availability which is important in making biofilms. We used dyes to measure the effect of the chelator in grown biofilms. The treatment showed an increased antibiotic effectiveness against biofilm when they are combined with the iron chelator.

SHAPING THE VACCINE AGAINST *CHLAMYDIA TRACHOMATIS*

Emily Chan
Supervisor(s)/Collaborator(s): Natalie Strynadka, Bronwyn Lyons, Robert Brunham, Hong Yu

Chlamydia trachomatis is the most common sexually transmitted bacterium worldwide. Despite the antibiotic treatments and control methods used to manage infections, most chlamydia infections do not show symptoms and the infection rates of *C. trachomatis* continue to rise globally every year. Currently, there are no vaccines available; therefore, the development of a vaccine is necessary to protect individuals prior to becoming infected with *Chlamydia trachomatis*. OmpA is an outer membrane protein from *C. trachomatis* that is a potential vaccine target because it can trigger an immune response within the host. For this project, we investigated the structure of OmpA. The workflow to purify OmpA was optimized to acquire enough proteins required to determine the structure of OmpA. Electron microscopy images that we obtained for OmpA revealed that OmpA assembles into groups of three and forms a ring-like structure with a pore at the center. Further structural studies will be pursued during vaccine development to obtain atomic details of OmpA for optimizing the effectiveness of the vaccine against *C. trachomatis*.

ELUCIDATING THE RELATIONSHIP BETWEEN CD248 AND PDGF IN TYPE II DIABETES

Emmanuel Garrovillas
Supervisor(s)/Collaborator(s): Andy Hsu, Edward Conway

Type II Diabetes (T2D) is a common, multisystem inflammatory disease, characterized by sugar level dysregulation. This comes with many complications, such as altered adipogenesis (i.e., fat tissue formation) and vascular diseases. Associated with T2D is a protein called CD248, which is found at high levels in T2D and vascular diseases. Interestingly, a lack of CD248 has been found to protect against diabetes in mice, but the underlying mechanism is unknown. Platelet-derived growth factor (PDGF) is another molecule known to participate in vascular diseases and regulate adipogenesis, so we hypothesized that CD248 may regulate PDGF signalling pathways, aiding in T2D progression. We determined that there is likely both a spatial and functional relationship between CD248 and PDGF signalling. Future directions include determining how CD248 and the receptor for PDGF physically interact and what the physiological relevance of this interaction, which will hopefully lead to exploring CD248 as a potential therapeutic target for T2D.

USING THE EVOLVER AUTOMATED CELL CULTURE PLATFORM TO INVESTIGATE PHAGE-HOST DYNAMICS AND EVOLUTION DURING CHANGES IN OSMOLALITY

Eric Lyall
Supervisor: Carolina Tropini

The gut microbiota hosts hundreds of bacterial, viral and fungal species which play a critical role in our health and well-being. Prior research indicates changes in osmolality - in humans often due to osmotic diarrhea or laxatives - can significantly alter the composition of gut bacteria, causing species to rapidly adapt or become eradicated. Interestingly, some bacteriophages (or phages, bacteria-targeting viruses) attack cells via osmotic-sensing channels that are upregulated during osmotic stress. We hypothesize that the combination of changes in the osmotic environment and the presence of phages drives bacterial evolution during these osmotic shocks.

RNA THERAPY FOR THROMBOTIC DISORDERS

Francesca Ferraresso
Supervisor: Christian Kastrup

Thrombosis is the underlying cause of heart attacks and strokes; it affects more than 100,000 Canadians every year and of those more than 10,000 people die. Patients suffering from thrombotic disorders are administered anticoagulants, which inhibit thrombosis however significantly increase the risk of hemorrhage. In an attempt to balance the risk of thrombosis with that of hemorrhage, clinicians often face difficult decisions upon administration. Therefore, the development of new anticoagulants is needed.

Blood coagulation factor XII (FXII) has recently been found to play a primary role in thrombus formation but not in hemostasis. We hypothesized that a reagent which decreases FXII levels could provide a novel way to manage thrombosis without increasing the risk of hemorrhage. We formulated a siRNA-lipid nanoparticle reagent which targets FXII in the liver where it is synthesized. Mice were injected with the formulated reagent followed by an analysis of the FXII mRNA expression levels in the liver, and of the FXII antigen and activity levels in blood directed to evaluate the strength of the reagent and its ability to decrease FXII. Our results show that the newly developed siRNA-lipid nanoparticle reagent leads to a potent decrease of FXII levels in mice. Currently the anticoagulant potentiality of the siRNA-lipid nanoparticle is being tested in two thrombotic disorder animal models.

MITOCHONDRIAL DNA MUTATIONS OF SORTED LYMPHOCYTES IN PEOPLE LIVING WITH HIV AND NOT

Hailey Chapman
Supervisor(s)/Collaborator(s): Loïc Caloren, Hélène Côté

People living with HIV seem to age faster than people without HIV as they seem to get age-related diseases earlier in life. We don't yet know exactly how and why this is the case, but one possibility has to do with mitochondrial DNA mutations.

As we age, we have an increase in mutations in our mitochondrial DNA (mtDNA). In this study, I want to see how HIV infection might be related to this increase in mtDNA mutations. Specifically, I am looking at mtDNA mutations in different types of white blood cells. This has never been done before! White blood cells play a critical role in our immune responses, and they are important for both HIV infection and our bodies' response to it. Because immune cells have different roles in the immune system and immune cells change with age, I expect to see differences in the amount of mtDNA mutations. To do this, I am using a very precise sequencing assay (Primer ID - Next Generation Sequencing) which will allow me to measure very rare mutations.

This project will allow me to see how mtDNA mutations are different in individual types of white blood cells, and how HIV infection is related to mtDNA mutations in these cells. This may help us better understand how the immune system evolves with age and why people living with HIV age faster. This is important to understand the mechanisms behind this accelerated aging to improve treatment and quality of life in people living with HIV.

CUSTOMIZABLE FLEXIBLE 3D PRINTED EEG CAP AND ELECTRODES

Han Nguyen
Supervisor(s)/Collaborator(s): Cidnee Luu, Saeid Soltanian, Peyman Servati, Mike Van der Loos, Lyndia C. Wu

Electroencephalogram (EEG) has been widely used these recent decades to understand more how our brain works, diagnose mental diseases, and help the disabled or paralyzed by "translating" human thoughts into controlling commands. Commercially available EEG headsets or caps tend to be expensive, not fit the head, fragile, and uncomfortable to wear for a long time. Therefore, we designed a 3D-printable flexible EEG cap that can be customized based on the user's head dimensions, flexible dry, and flexible gel electrodes so that the EEG system will be more affordable, sturdy, having good signal quality even during movement, and more comfortable to be worn for a long time.

The wearable EEG system has been being tested on different participants by check the impedance of electrodes, finding alpha ratio of EEG between eye closing and eye opening, P300 due to audio oddball stimuli, and P100 while looking at a flashing screen. The test is done in both sitting still and during movement (walking, running, and jumping).

PROBING SIGNALING IN PLATELETS DURING ENDOCYTOSIS

Hoanne Chan
Supervisor(s)/Collaborator(s): Manoj Paul, Hugh Kim

Platelets are tiny blood cells that are responsible for blood clotting. When platelets are "activated" by a signal such as a cut or injury, platelets change shape, stick together, forming a blood clot. In addition to changing shape, activated platelets take in molecules from their environment through a process known as endocytosis. The processes of platelet activation and endocytosis are controlled by the cell's actin cytoskeleton, which is continuously remodeled and which provides structural support for the cell. The actin cytoskeleton is also controlled by a number of other proteins, including gelsolin, which is essential for actin remodeling. The goal of my project was to determine how proteins such as gelsolin control the signaling events that take place in platelets during endocytosis.

VALIDATION OF HUMAN ISLET CALCIUM-REGULATED GENES AND SUBTYPE MARKERS

James (Hyun Ku) Chae
Supervisor: Samantha Jisoo Yoon

Pancreatic human islets are composed of multiple cell types that detect and respond to changing blood glucose levels by secreting hormones. In these cells, calcium signaling is critical for normal function, including gene expression. In order to study the effects of calcium signaling in human islets, we previously used single cell RNA sequencing to identify all calcium-regulated genes in islet cell types. From this dataset, we found the gene *PCDH7* specifically marks insulin-secreting beta cells with enhanced function and the most calcium-regulated genes. To validate this finding, I used immunostaining to show that PCDH7 protein is in the same beta cells as NPAS4, a known calcium-regulated protein. I also used qPCR to confirm calcium-regulated gene expression in human islets. The study of differences in gene expression in islet cell subtypes may help provide insights on the biology of healthy islets, to better understand what happens when they malfunction.

NON-SPECIFIC RNA CLEAVAGE OF CRISPR-Cas13d IN MAMMALIAN CELLS

Janella Schwab
Supervisor(s)/Collaborator(s): Kieran Maheden, Nika Shakiba

Since their discovery, CRISPR-Cas systems have gained quick leverage as precise gene editing systems and have been further explored and modified to show promise in human clinical applications like gene therapies. CRISPR's precise and programmable nature relies on the activity of Cas proteins, which are directed to cleave a user-specifiable region of genetic material. However, some Cas proteins can unintentionally bind to un-targeted regions of genetic material, causing collateral damage of random sequences after the initial target cleavage, which can have severe consequences for the health of the cells and limits the use of CRISPR systems. Such is the case for Cas13, a Cas protein noteworthy for targeting and binding to RNA instead of DNA. Although the collateral cleavage activity of Cas13 has been well documented in bacterial cells, the effect in human cells is poorly understood, which is critical for evaluating the reliability of Cas13-based clinical application technologies. We aimed to report whether CRISPR-Cas13 induces collateral cleavage in human embryonic kidney cells, through tracking on-target versus collateral Cas13 activity on fluorescent proteins at single cell resolution using flow cytometry. This demonstrated robust collateral cleavage of non-targeted fluorescent proteins, which encourages reevaluation of the use of target specificity of Cas13 nucleases for human research applications until the source of this collateral activity can be understood and addressed.

HARNESSING VERTEBRATE V(D)J RECOMBINATION TO DEVELOP A NEW HIGH-RESOLUTION CELL LINEAGE TRACING TECHNOLOGY

Jennifer Jiang
Supervisor(s)/Collaborator(s): Soh Ishiguro, Nozomu Yachie

"DNA event recording" systems, by which synthetic DNA barcode arrays are stably integrated into the chromosome and continuously accumulate mutations via genome editing during cellular division, can be used to decipher how every cell divide and differentiate through the entire course of mammalian development. However, current systems have limited resolution for lineage reconstruction. To combat this issue, we aim to develop a more scalable, autonomous event recording circuit by mimicking V(D)J recombination: an essential process for vertebrate immunity that is responsible for generating millions of highly-specific antibody-encoding sequences by double-stranded DNA breakage and reassembly of the recombination signal sequence (RSS), with the help of recombination-activating gene (RAG) proteins and the terminal deoxynucleotidyl transferase (TdT). We hypothesized that this process could be used to generate diverse DNA barcode sequences in a cell, which could be used as an alternative high-resolution cell lineage tracing tool. The goal of my summer research project is to develop a reporter system which validates successful *in vivo* V(D)J recombination events. To date, I have successfully synthesized a dual-color fluorescent reporter plasmid by performing molecular cloning and assembly. The reporter encodes two fluorescent proteins with the RSS recognition sequence for RAG and TdT. Upon cellular transfection, four different color combinations can be expressed depending on which V(D) J cellular event happened. The next step is to assess the precision of this reporter by performing and analyzing cellular V(D)J recombination assay. This project will be the first step towards the development of a new high-resolution cell lineage tracing technology.

MODELLING AND CONTROL AND STEM CELL SIGNALLING DOMAINS

Jonathan Gui
Supervisor(s)/Collaborator(s): Daniel-Aguilar Hidalgo, Peter Zandstra

Growth and development are guided by diffusible signalling gradients formed by self-organizing molecules known as morphogens. Morphogens form patterns of signalling activity throughout growth and instruct the differentiation of cells towards specialized types, with specific characteristics and functions. Patterns in experimental stem cell colonies vary in shape and size with the size of the colony, but we have discovered a scaling correlation between the sizes of colonies and expression domains of Brachyury, an early mesodermal marker, within mouse pluripotent stem cell (mPSC) colonies. In addition, we have observed and measured a signalling domain growth rate which is collectively followed by all colonies, independent of their size. From our quantifications, we have developed a model of Brachyury expression domain growth, based upon an activation-threshold of the upstream morphogen BMP. Simulations of this model agree with the types of dynamics observed experimentally, and may help further our understanding of the way morphogens influence differentiation and tissue growth.

CLONAL INTERACTIONS BETWEEN NORMAL AND ABNORMAL HUMAN STEM CELLS

Karen Hwang
Supervisor(s)/Collaborator(s): Omar Bashth, Nika Shakiba

Human pluripotent stem cells (hPSCs) are used in a diverse range of therapeutics since they can replicate indefinitely as well as the flexibility to become any other cell type. hPSCs are commercially grown in large bioreactors, but DNA mutations cause abnormal cells to emerge, which overtake the population and make an entire batch of cells unusable. This leads to a waste of time, money, and resources. Previously, it was assumed that abnormal cells took over the population only because of a growth advantage. However, it has recently been shown that abnormal cells "bully" and kill normal stem cells through contact-dependent interaction. To quantitatively prove the impact of culture conditions on interactions between normal and abnormal cells, we integrate blue and green fluorescent proteins into their DNA, then seed the cells together at different densities. Seeding densities impact access to nutrients and space, colony formation, and cell-cell signalling. We then use fluorescence microscopy to take snapshots of the cells over six days to monitor cell-cell contacts. Image analysis allows us to quantify interactions between normal and abnormal cells as well as to measure population size over time. In the next stage of our project, we will be exploring how different seeding ratios impact the ability for normal and abnormal cells to interact. By identifying how controllable parameters in the culture impact the ability for abnormal cells to interact with, and therefore bully normal cells, we can optimize these bioprocess parameters to curb the ability for abnormal cells to overtake the culture.

ROLE OF PRG-1 PALMITOYLATION IN SYNAPTIC PLASTICITY

Kira Tosefsky
Supervisor(s)/Collaborator(s): Shernaz Bamji, Angela Wild, Glory Nasseri

Synaptic plasticity describes strengthening or weakening of connections between neurons and serves as the molecular basis for learning and memory. Alterations in the strength of synaptic connections are mediated by changes in neuronal protein activity, localization, and expression. One mechanism by which these changes occur is through the attachment of lipid groups to proteins. Palmitoylation refers to a type of reversible protein lipid modification that anchors proteins to biological membranes and influences their trafficking between cellular compartments. Over 40% of synaptic proteins are substrates for palmitoylation, and accumulating evidence has pointed to palmitoylation as a potentially critical regulator of synaptic plasticity. To further investigate the relationship between synaptic protein palmitoylation and plasticity, my summer project examined the effect of blocking the palmitoylation of a plasticity-implicated protein, PRG-1, on activity-dependent synapse strengthening. I found that preventing PRG-1 palmitoylation reduced the magnitude of excitation-induced synapse strengthening in cultured rat hippocampal neurons. However, this effect was not explained by a change in the localization of PRG-1 at the synapse. Further work will be required to elucidate an alternate mechanism by which palmitoylation of PRG-1 acts to increase the efficacy of synaptic plasticity and thereby regulate learning and memory.

VISUALIZING THE SPATIAL ORGANIZATION OF GUT BACTERIA

Kisa Naqvi
Supervisor(s)/Collaborator(s): Jen Nguyen, Carolina Tropini

Bacterial communities in the human gut are diverse, containing hundreds of bacterial species spatially organized into a complex ecosystem. Understanding the specific location of these species provides insight into their interactions and functions in the gut. For example, many intestinal pathogens (such as *Salmonella*) must contact the gut epithelium to trigger inflammation. The ability to observe how bacterial spatial organization changes over time is essential to understanding how bacteria influence human health. Current microscopy methods are limited by the number of different bacterial species that can be visualized at the same time. To overcome these limitations, recent methods (*e.g.*, HiPR-FISH) employ combinations of fluorescent DNA probes for simultaneous labelling of single cells in complex communities. We built on these methods, with the goal of creating a tool for visualization of over 50 different bacterial species. To pursue this aim, we first used a computational tool, OligoMiner, to design unique probes to target specific DNA sequences in each species. We tested each probe against every bacterial strain to quantify on- and off-target labelling by measuring the fluorescence intensity from pure fixed bacterial cultures. In determining the specificity of these probes, the project contributes a well-characterized resource for visualizing the spatial structure of bacterial communities in diverse guts. This tool can answer fundamental questions, such as which species interact together and where these interactions occur. These answers will propel our understanding of how diverse communities of gut bacteria contribute to complex human conditions, such as inflammatory bowel disease and intestinal infections.

TAK1 SIGNALING IN MESENCHYMAL STEM CELLS REGULATES THE TYPE 2 INFLAMMATORY RESPONSE

Lucas Rempel
Supervisor(s)/Collaborator(s): Fabio Rossi, Marine Theret

The inflammatory response is a key determinant of whether our body's response to an insult will lead to regeneration or to the further loss of tissue function. A simplified model of the inflammatory response distinguishes between a "type 1" and a "type 2" response, with the first usually exacerbating damage through the action of aggressive inflammatory cells, and the second limiting the damage but potentially leading to the deposition of interstitial extracellular matrix that may interfere with healing. Each organism is predisposed to respond in one or the other way, and others and our prior work suggests that mesenchymal stem cells (MSCs) are critical in determining the prevalent type of response. This is thought to occur between communication with immune cells, however, the mechanism through which this occurs is unknown. In our experiments, we have identified TGFb-Activated Kinase 1 (TAK1) as a factor in MSCs that dictates the prevalent type of inflammatory response, specifically, $MSC^{TAK1\text{-}KO}$ mice are skewed towards a strong type 2 response. Our project takes advantage of these TAK1 KO mice to study type 2 inflammation and how the communication between MSCs and the immune system may regulate its systemic effects. A better understanding of this communication may help in the development of future MSC-based therapies to treat diseases with a significant inflammatory component, such as asthma, Graft versus Host Disease, and diabetes.

MICROSCOPIC EXAMINATION OF TRANSMEMBRANE PROTEIN HELPS PREDICT CYSTIC FIBROSIS TREATMENT OUTCOMES

Lydia Li
Supervisor: Ivan Robert Nabi

Cystic fibrosis is a disease caused by mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene and leads to persistent lung infection. However, only 25% of patients respond to the targeted gene therapy for a CFTR mutation hindering protein transport to cell membrane and the drug is prohibitively expensive. Therefore, we aimed to investigate how mutations impact CFTR distribution on cell surface and patient response. By analyzing molecular scale microscopy images of cells carrying different CFTR mutations, we discovered differences in number and size of CFTR cluster on cell membrane. Our findings suggest CFTR distribution in patient cells may predict treatment outcomes.

PROMOTING NERVE FIBER GROWTH AFTER A SPINAL CORD INJURY

Max Arsenault
Supervisor: Dena Shahriari

Spinal Cord Injuries (SCIs) are a prevalent issue worldwide, with hundreds of thousands of people being diagnosed each year, and no effective cure available. SCIs occur when nerve fibers in the spinal cord are damaged, preventing signals from passing between the brain and body. This causes paralysis among other complications. One of the issues in obtaining functional recovery after an SCI is that the nerve fibers do not spontaneously regenerate after an injury. Two drugs' roles are examined separately for their efficacy to promote nerve fiber growth after an SCI. The first drug, a growth factor, is required to be present in consistent, continuous quantities at the injury site for many days. An adhesive is used to bind the growth factor to a surface to slow down its release, promoting nerve fiber growth after an SCI. The second drug explored, a natural cell adhesion peptide sequence, is immobilized such that it does not release from a surface. This peptide sequence will adhere to nerve fibers, promoting their growth along the spinal cord. Further investigation into these two growth promotion methods will lead to continued findings in nerve fiber growth after an SCI.

STRUCTURAL DETERMINATION AND ANALYSIS OF SAR-COV-2 M^{PRO}

Myles Ng
Supervisor(s)/Collaborator(s): Natalie Strynadka, Marija Vuckovic, Jaeyong Lee

Secure Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), better known as COVID-19, contains a collection of proteins. Nsp5 is the main protease (M^{Pro}) has a critical role in the function and reproduction of COVID-19, responsible for cutting at 11 locations. There is an amino acid within M^{Pro} important for its function, a cysteine located 145 residues in the sequence. To fully understand how M^{Pro} works, its interaction with each of the 11 sites should be examined, as the sites are similar to one another but are not identical. Therefore, a wildtype (WT) and a mutant (C145A) were used. The C145A mutant features an alanine residue instead of the cysteine, killing its function. The objective of the project is to crystallize M^{Pro} whilst it has one of the 11 sites bound. To do so, we use bacteria to produce the appropriate M^{Pro} before isolating the protease, crystallizing it, and solving the structure. The resulting data from the 22 combination will show how M^{Pro} binds onto its target and have implications on drug development.

BIOMATERIALS-BASED SCAFFOLDS TO GUIDE AXONAL GROWTH AFTER SPINAL CORD INJURY

Nadine Truter
Supervisor: Dena Shahriari

Spinal cord injuries affect the lives of millions worldwide, causing paralysis, organ function loss, and more, yet no effective treatment currently exists. The injury causes damage to the nerve cells in the spinal cord, which are responsible for relaying messages from the brain to the body and vice versa, and these do not regenerate spontaneously. For their regeneration, and thus the treatment of spinal cord injuries, these cells require physical guidance to direct their growth across the injury site to reform the damaged cellular connection. My work is focused on developing injectable scaffolds in the form of multiple singular, hollow channels that will physically guide and direct these cells, once stimulated, to grow across the injury site in the spinal cord. After injection, the channels will not yet be correctly oriented and thus must be properly aligned to guide the growing cells in the correct direction. This is achieved by embedding small magnetic particles in the channels and aligning them post-injection by applying a magnetic field to the channels. The ultimate goal of these injectable channels is to allow the lost connection between the cells in the spinal cord to be re-established.

EXPLORING THE POTENTIAL OF CONVALESCENT PLASMA THERAPY AND OTHER EXPERIMENTAL THERAPIES AS AN INTERVENTION IN THE PANDEMIC RESPONSE; CONCOR-1 AS A CASE STUDY

Parvin Malhi
Supervisor(s)/Collaborator(s): Andrew Shih, Krisztina Vasarhelyi, Maya Gislason

Early in the course of an outbreak, when efficacious treatments and vaccines are lacking, prompt action is critical to prevent or delay the exponential growth of infections. One early COVID-19 treatment that underwent rigorous assessment in randomized clinical trials is convalescent plasma. Convalescent plasma contains antibodies and other blood factors from a previously infected individuals that putatively boost immunity in recipients. This therapy was used in the CONCOR-1 Canada-wide clinical trial. The logistics of finding the right donors, ensuring regulatory requirements are met, having hospitals equipped and prepared to infuse plasma in the setting of a clinical trial, and distributing plasma effectively are all challenges faced by the health care system during this pandemic.

The purpose of this case study is to follow the implementation of CONCOR-1 in British Columbia in order to inform future pandemic planning, specifically to learn how the health care system can continue to improve so that convalescent plasma and other experimental therapies can reach the right patient in a timely, safe and equitable manner. The end product of this study is to process map the delivery of convalescent plasma within CONCOR-1 from identifying donors to preparing hospitals by stakeholder engagement. In addition, the qualitative data generated in this study will be used in the development of a knowledge translation package that can be used a guide by researchers in future pandemics. To collect the data, semi-structured interviews with key stakeholders including CONCOR-1 trial staff, public health physicians, and Canadian Blood Services representatives are being conducted.

EDUCATING SCIENTISTS ON RISK COMMUNICATION IN A PUBLIC HEALTH EMERGENCY

Puneet Sidhu
Supervisor(s)/Collaborator(s): Jenna Usprech

Risk communication is an important part of health policy development, especially in a public health emergency like the COVID-19 pandemic. Educating scientists on the best practices of risk communication can provide them with beneficial skills for translating their work and research into effective communication for a variety of audiences. Scientists themselves require these skills to ensure that different audiences, especially policymakers, are accurately informed on evidence-based research. However, scientists working on research relevant to public health emergencies are not traditionally taught about health policy and risk communication. In this project, a review of literature on risk communication was performed in conjunction with interviews of policy professionals and health researchers to identify the goals and best practices of risk communication. This research was then translated into a risk communication and health policy lesson plan for undergraduate and graduate students. The lesson plan involves an explanation of health policy, investigation of risk perception, description of the best practices of risk communication, and finally an analysis of risk communication strategies used in the COVID-19 pandemic. Educating young scientists on risk communication and health policy is vital to ensure effective communication of evidence-based research in public health emergencies.

THE ROLE OF PLATELET FACTOR 4 (PF4) IN RHEUMATOID ARTHRITIS

Quan Nguyen
Supervisor(s)/Collaborator(s): Michael Hughes, Hugh Kim, Kelly McNagny

Rheumatoid Arthritis (RA) is an inflammatory disease leading to swollen joints and pain. It is the leading cause of disability worldwide and affects about 1% of adult Canadians. Platelets are cells in the blood that are needed for blood clotting, and platelet factor 4 (PF4) is a major protein that is released by platelets. However, the role of platelets and PF4 in inflammation, and specifically in RA, are not clearly understood. To study the role of PF4 in RA, we induced RA in wild-type ("regular") mice as well as mice engineered to be PF4-free (knockout mice) and monitored for joint inflammation. Our results show that the knockout (PF4-free) mice had less joint inflammation and tissue damage than did the wild-type mice. Consequently, the data suggest that platelets (and PF4) play a role in joint inflammation seen in rheumatoid arthritis.

CLINICOPATHOLOGIC CHARACTERISTICS AND TREATMENT OUTCOMES OF PLASMABLASTIC LYMPHOMA IN BRITISH COLUMBIA

Rehan Jessa
Supervisor(s)/Collaborator(s): Alina S. Gerrie, Nicole Chien

Plasmablastic lymphoma (PBL) is a rare and aggressive blood cancer. Initially recognized in HIV positive patients, PBL presents with rapid symptom onset and is associated with poor survival outcomes. Currently, there is no standard treatment for PBL and clinical research studies have been limited due to the rarity of the disease. To better understand the clinical characteristics and treatment outcomes associated with PBL, a retrospective cohort review was conducted including all PBL cases diagnosed in BC between 1997 and 2019. Overall, 42 patients were identified. The majority were male (83%), immunosuppressed (36% HIV positive, 21% other immunosuppression) and had advanced stage disease (69%). 31 patients were treated with an intent to cure their disease. Following treatment, only 51% of patients survived longer than one year and only 47% survived one year without their disease progressing. There was no difference in survival outcomes between patients with normal or weakened immune systems. Findings confirm that PBL is difficult to treat and suggest low cure rates and poor survival irrespective of immune system function. Ultimately, further research is necessary to understand the biologic mechanisms behind progression of PBL and to develop more effective treatment strategies for the disease.

CHARACTERIZING FUNCTIONAL IMPACTS OF ACE2 RECEPTOR VARIANTS ON COVID-19 DISEASE PATHOPHYSIOLOGY

Ryan Hong
Supervisor(s)/Collaborator(s): Warren M. Meyers, Wun Chey Sin, Kurt Haas

Angiotensin-converting enzyme 2 (ACE2) is an enzyme that is expressed on the membranes of cells, located in several places throughout the body, including the heart, lungs, arteries, kidneys and intestines. Upon COVID-19 infection, the SARS-CoV-2 virus uses ACE2 to facilitate entry into cells, and in doing so, downregulates ACE2 expression which will deplete ACE2 on the surface of human cells driving injury and inflammation; hence, resulting in disease phenotypes seen in COVID-19 patients and other comorbidities including hypertension, diabetes, and chronic obstructive lung disease. Therefore, a holistic understanding of the molecular mechanisms underlying COVID-19 pathophysiology requires knowledge of the binding interaction between SARS-CoV-2 variants of concern with ACE2 variants and screening the impact of genetic variation on ACE2 protein structure and function. To study this, I am creating variants of ACE2 and transiently expressing them in HEK293 cells to perform multi-functional assays that look at stability, expression, binding, and enzymatic. Our research findings will allow us to create a platform for rapid functional assessment of SARS-CoV-2 variants to study the extent at which genetic variation in the ACE2 gene may contribute to COVID-19 expression so that we can integrate both clinical and genetic information to personalize our approach to COVID-19 patients.

A META-ANALYSIS OF COVID-19 DISEASE OUTCOMES

Simranpreet Mann
Supervisor(s)/Collaborator(s): Amani Abid, Bhavjinder Dhillon, Robert E. Hancock

COVID-19 is a respiratory disease that has caused a worldwide pandemic and has resulted in the death of over 3.93 million people. It is caused by a virus known as SARS-CoV-2.

Hospitalized COVID-19 patients are categorized by disease severity into mild, moderate, and severe groups, as determined by SOFA scores and APACHE II scores. However, current research has shown SOFA and APACHE II scores to be ineffective in predicting COVID-19 disease outcomes in ICU patients.

In this study, we conducted a meta-analysis, a type of quantitative review, of the current literature discussing molecular differences between hospitalized COVID-19 survivors and non-survivors. Despite the widespread effect of SARS-CoV-2 globally, current research is limited by small sample sizes. Therefore, we performed a meta-analysis across multiple studies to identify baseline characteristics associated with mortality in hospitalized patients.

We used a PubMed search and identified 7 studies eligible for inclusion in this review. Laboratory findings from blood taken from patients in the hospital were extracted from each study. We estimated the mean and standard deviation (SD) for each study. The Cochrane RevMan 5 software was used for all statistical analyses.

When comparing hospitalized COVID-19 survivors and non-survivors across these studies, the analysis reveals significantly higher platelet levels in survivors, while IL-6, creatinine and C-reactive protein levels were higher in non-survivors. Future work includes meta-analysis of comparable transcriptomics studies to identify shared gene expression changes that could also be used to further predict COVID-19 disease outcomes and provide insights into early interventions/treatments.

CHEMICALLY INDUCED KIDNEY FAILURE IN PODOCALYXIN HETEROZYGOUS MICE

Yasmine Yuen
Supervisor(s)/Collaborator(s): Michael Hughes, Kristen Li, Kelly McNagny

Glomeruli are our kidney's functional filtration centres for blood. Podocalyxin protein (podxl) is expressed at these balls of capillaries, which are wrapped in podocyte cells. Podxl is integral to kidney development and function, and healthy individuals have two copies of podxl genes. However, individuals with one copy (heterozygous) are susceptible to fatal kidney disease– this is the leading cause of kidney transplants. Indication of disease is most effectively detected through protein leakage in urine. We hypothesized either podocytes or capillary tissues heterozygous for podxl are responsible for chemically induced kidney disease. Therefore, we used several strains of mice as models to determine which podxl heterozygous tissues are paramount to this susceptibility. On day 0, drug was administered to the mice to induce kidney failure. Urine was collected on days 0, 7, and 14, and blood was collected on day 14. Subsequently, we measured the protein levels in the urine and blood. Results revealed mice heterozygous in podocyte cells had significantly elevated levels of blood protein in their urine while capillary heterozygous mice showed minimal to no protein. Thus, we concluded that one copy of podocalyxin in podocytes causes susceptibility to induced kidney failure. To investigate how podocalyxin heterozygosity affects the kidney function, further research will involve verification of these results with a larger sample size and sequencing the relevant genetic material to reveal potential mechanisms.

SUMMER STUDENT EXPERIENCES & PERSPECTIVES

"The objective of my project was to analyze clinical and genetic parameters of patients with Juvenile Idiopathic Arthritis (JIA), in order to determine predictors of intolerance to the first line treatment of the disease, methotrexate.

I got to work closely with Dr. Martina Sundqvist of the Brown Lab at BC Children's Hospital Research Institute, who was an excellent mentor and guide in my first paid research experience. The program workshops, despite the online format, truly exhibited a care for the professional development of us summer students. CBR Research Day was an especially enjoyable time, allowing me to give a research presentation for the first time, as well as see all the interesting projects the other students had worked on this summer!"

— Rafid Haq,
2020 CBR-SBME Summer Student alum

"All in all, the CBR-SBME Summer Studentship Program was a hub of unforgettable opportunities."

"This summer could not be complete without Dr. Jenna Usprech's brilliant guidance – she made my first research project a truly memorable experience. All in all, the CBR-SBME Summer Studentship Program was a hub of unforgettable opportunities. I especially enjoyed the professional development workshops and seminar series on current CBR research.

Despite the unprecedented nature of 2020, this program stayed just as organized and aware of its students and supervisors' needs, which I appreciated. Seeing such a small community come together (virtually) and share their progress during Research Day was very inspiring!"

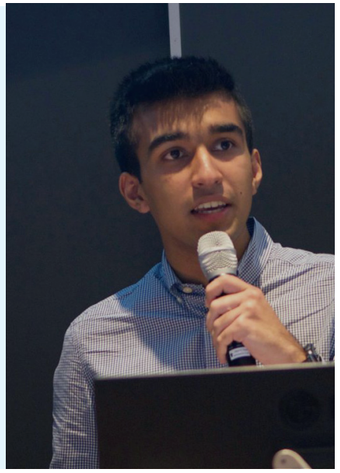
— Polina Petlitsyna,
2020 CBR-SBME Summer Student alum

"As someone who recently finished his first year of undergraduate studies and had no prior research experience, I cannot thank the Centre for Blood Research (CBR) enough for the opportunity to get an early start in clinical research and develop my skills.

Working daily with post-graduate medical residents under the supervision of a staff physician has taught me so much about what it takes to be successful, not only in clinical medicine, but in academia. The unparalleled guidance and mentorship I have received from Dr. Andrew Shih, Dr. Bhupinder Johal and Dr. Ann Tran, has made me realize that medicine and research is something I would pursue after my undergraduate studies.

I feel that the meaningful professional relationships I have built will serve me very well in making sure those dreams are a reality."

— Amardeep Sekhon,
2019 CBR-SBME Summer Student alum



"The unparalleled guidance and mentorship I have received ... has made me realize that medicine and research is something I would pursue after my undergraduate studies.

I feel that the meaningful professional relationships I have built will serve me very well in making sure those dreams are a reality."

"Before this summer, I knew very little about research and academics outside of the classroom, but I have now found a new/renewed love for science and research. I did my summer research project titled "Modulation of the Immune System as possible therapy for Muscular Dystrophy" in the McNagny Lab.

Being able to prepare and present my work to my peers and other scientists at Research Day was very beneficial. It was not only great practice of my presentation skills, but it tested my understanding of the work I had done, and I am so honoured to have been awarded the People's Choice Award. Furthermore, attending scientific conferences and meetings added another layer to an already holistic experience.

I truly appreciate all the CBR and SBME staff, as well as the McNagny Lab, for all their amazing support and direction."

— Sia Cecilia Jan-Abu,
2019 CBR-SBME Summer Student alum

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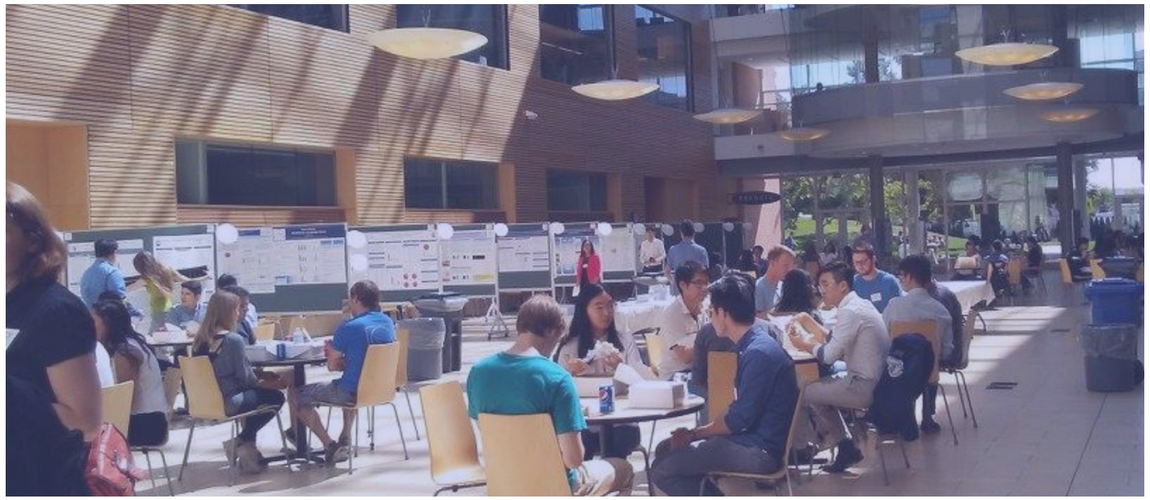

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