Michael Smith Health Research BC

2023 Trainee Award Recipients

Award Recipient	Host Institution / Research Location	Project Title	Lay Summary
Ifeoluwa Awogbindin **Supervisor** Marie-Eve Tremblay **Co-supervisor** Therese Di Paolo	University of Victoria Partner: Parkinson Society BC	The impact of SARS-CoV-2 infection/COVID-19 and microglial contribution on the development and severity of Parkinson's disease	Parkinson's disease (PD) globally affects 1 in 100 adults above 60. Exposure to environmental agents including viral infection increases vulnerability to PD. Hyperactivity of brain immune cells named microglia is also a strong determinant of PD onset and progression. Altered brain functions persist in patients during and after COVID-19. Evidence in the brains of patients who died of COVID-19 show dysfunctional microglia in brain areas affected by PD. These abnormal microglia were also observed in infected monkeys without breathing difficulty. In BC, where above 89% of total SARS-CoV-2 cases do not require hospitalization, older adults totaling 41% of the population, account for 31% of total cases. In mice, SARS-CoV-2 failed to multiply in microglia but initiated robust deleterious microglial functions, which were intensified by the exposure to PD-associated abnormal proteins. Thus, we propose that COVID-19 may precipitate PD onset or exacerbate its progression. We aim to study the impact of COVID-19 pathology on PD onset/progression and microglial implication in a mouse model expressing the human receptors of SARS-COV-2. This study will inform on COVID-19 long-term effects and may position microglia as a future therapeutic target.
Kelcey Bland **Supervisor** Kristin Campbell **Co-supervisor** Helen McTaggart-Cowan	University of British Columbia	Development of a patient-centred decision aid for rehabilitation in the advanced cancer setting	Advanced cancer and its treatment can lead to physical function declines and disability. Physical function is the ability to perform activities of daily living and patients with advanced cancer describe that addressing losses in physical function is a top care priority. Cancer rehabilitation is designed to improve physical function, yet available services are underutilized by patients with advanced cancer. Poor patient and healthcare provider (HCP) communication and ineffective shared decision making about rehabilitation are key reasons for this care gap. Decision aids (DAs) are tools that enhance shared decision making, so patients know the decision to be made, understand options and outcomes, and have clarity on their personal values. Currently, a DA for cancer rehabilitation does not exist. The proposed research will develop a DA for cancer rehabilitation by determining patient decision support needs, designing a DA prototype, and evaluating the DA's usability. The DA is a simple and low-cost tool that may improve patient and HCP communication about cancer rehabilitation, so that the top care priorities of patients with advanced cancer are better addressed within the current healthcare system.
Faezeh Borzooee	BC Cancer	Targeting APOBEC3 enzymes as novel metabolic regulators in multiple myeloma	APOBEC3 are a family of molecules which mutate specific genes in the white blood cells of our immune system to boost immune function and defend against viruses. Unfortunately, they frequently make mistakes and target thousands of other bystander genes which are not

Supervisor Florian Kuchenbauer			their normal targets. These undesirable collateral mutations play a major role in both cancer initiation and progression. Multiple myeloma (MM) is an incurable disease whose progression depends especially on acquiring genetic modification, and indeed APOBEC3-mediated mutations have been shown to correlate with worst clinical outcomes. Beyond this association, it is unclear how APOBEC3 expression drives MM progression. Based on emerging hints in the literature, we hypothesize that APOBEC3s play at least two distinct roles in MM: first, they can cause mutations that impact the energy management of MM cells, and, second, that APOBEC3s can cause drug resistance mutations through which MM cells escape treatment. The goal of this proposal is to study the role of APOBEC3s in drug resistance and energy management of MM cells as well as to test if inhibiting APOBEC3s in MM may be of therapeutic benefit in cell-based and mouse model preclinical experiments.
Yu Chen **Supervisor** Filip Van Petegem	University of British Columbia	Structural and functional investigation of skeletal muscle calcium channels in health and disease	For muscle contractions to occur, electrical signals will travel from the brain to the muscle via a complex process. Two key players involved in this process are the voltage-gated calcium channel (Cav1.1) and ryanodine receptor 1 (RyR1). Cav1.1 senses the electrical signal and triggers opening of RyR1 to release calcium required for muscle contraction. When they malfunction, it can give rise to several muscle diseases, such as congenital myopathies, periodic paralysis, malignant hyperthermia, and central core disease. The proposed project will use advanced imaging techniques to look at three-dimensional structures of these proteins to understand the process of voltage-sensing. The project will also investigate how disease mutations, endogenous modulators, and pharmacological agents change the structure and function of these proteins. These structural and functional insights will help us understand the cause of these muscle diseases and provide a framework for design of novel therapeutics to prevent and treat them.
Tyrone Curtis **Supervisor** Nathan Lachowsky	University of Victoria	HIV prevention for underserved men who have sex with men: a community-based mixed methods exploration of access needs and preferences	Oral HIV prevention medications are highly effective and available at no-cost to clinically eligible patients in British Columbia. Men who have sex with men (MSM) remain a key population at a higher risk of HIV infection. However, studies suggest that certain sub-groups of MSM who would benefit from these medications are currently underserved. For example, MSM who identify as bisexual or heterosexual may be especially unlikely to use oral HIV prevention medications, leaving them and their sexual partners at higher HIV risk. Through analysis of community health survey data and one-to-one interviews with MSM in BC, my project will identify barriers to using PrEP among underserved MSM. I will explore their opinions about and preferences for different forms of HIV prevention, including oral and long-acting injectable forms of these medications. My research will help healthcare providers, community organizations and public health bodies to better understand the HIV prevention needs of underserved MSM. It will enable them to reach underserved MSM with information about ideal HIV prevention options, and to improve HIV prevention among this population, reducing the burden of HIV for these men and their partners.

Simon Dobri **Supervisor** Randy McIntosh	Simon Fraser University Partner: Alzheimer Society of BC	Multisensory integration in aging and Alzheimer's disease	As people age, their senses become less sharp. Healthy older adults can combine information from different senses, such as hearing and vision, to make up for this. Alzheimer's disease attacks the areas of the brain that combine sensory information. Because of this, Alzheimer's disease patients may lose the ability to compensate for reduced sensation. This could explain why Alzheimer's disease patients have a much larger risk of serious falls. For my project, I will study the brain activity involved in combining information across different senses. I will record brain activity from healthy young adults, healthy older adults, and Alzheimer's disease patients. The participants will perform a task requiring them to quickly and accurately combine visual and auditory information. I will compare recordings from the different groups to see how aging and Alzheimer's disease affect the brain activity. The information I learn from my project will inform approaches to treatment and accommodation. My ultimate goal is to help people live fuller, more independent lives as long as possible.
Sarah Faber **Supervisor** Randy McIntosh	Simon Fraser University Partner: Alzheimer Society of BC	Mapping the musical brain in dementia	Music is an important part of life for individuals with dementia and their loved ones. Numerous clinical studies have detailed music's positive effects on quality of life in dementia care, however, much is still unknown about how music is processed in the brain, and how the brain adapts to neurodegeneration in dementia to maintain a connection to music. This is an important unanswered question as many assessment tools do not allow us to look at brain activity with persons with dementia in a way that is enjoyable and accessible to the individual. This project will record brain data during music listening and analyze the resulting brain network data for age- and diagnosis-related patterns. Music helps stimulate memories and promotes social interaction with loved ones, making it a beneficial addition to the lives of individuals with dementia. However, much still needs to be discovered about how and why music works. This study will provide information that can help improve access to music-based therapies for individuals with dementia in BC and will give researchers a greater understanding of brain adaptation in dementia.
Flora Foltanyi **Supervisor** Filip Van Petegem	University of British Columbia	Structural and functional investigation of the skeletal muscle excitation-contraction coupling complex	This project aims to understand the basic function of the skeletal muscle, and how mistakes in this function can lead to life-threatening disease. A key element of the complex biochemical process known as muscle contraction is a specific particle, named calcium ion. Both the heart and skeletal muscle tissues rely on the movement of calcium ions within each individual muscle cell. This movement occurs through specialized proteins that form 'pathways' or 'channels'. When this pathway does not work properly, however, there can be deadly consequences. In the heart, for example, mutations in the DNA can lead to faulty channel proteins that can no longer allow the normal passage of the calcium ions. This leads

			to heart rhythm disorders that can result in sudden cardiac death. How exactly the mutations cause this is not fully understood. We aim to understand this, by looking at the detailed 3-dimensional structure of the pathway, and by comparing healthy proteins with diseased versions. Because proteins are too small to see with the naked eye or even with very good light microscopes, we need to use a special tool. We will make use of a so-called 'electron microscope', whereby the protein is bombarded with electrons instead of light.
Vanessa Fong **Supervisor** Jennifer Baumbusch	University of British Columbia	Improving the Healthcare Experiences of Racialized Newcomer Families of Children with Medical Complexity: A Qualitative Longitudinal Study	Racialized (e.g., Chinese, South Asian) newcomer (e.g., arrived in Canada within 5 years) families experience greater challenges accessing healthcare services for their children with medical complexity (MC). This contributes to unmet healthcare needs and higher rates of hospitalizations, emergency department visits, and readmissions. Yet despite this, there is very little research on the healthcare experiences of racialized newcomer families. In order to learn about these experiences, we will look at organizational- and provincial-level policies to see if they address the needs of these families. We will interview caregivers and have them complete diary entries about their experiences over time. Using what we learn from this research, we will co-develop recommendations with families that address their unique needs. We will share the results with policy-makers, clinicians, and other knowledge users to help improve healthcare services for racialized newcomer children with MC and their families.
Liam Hall **Supervisor** James Johnson	University of British Columbia	New Connections Between Insulin and Exercise	Obesity and type 2 diabetes are significant public health issues, with 31% of British Colombians living with prediabetes or diabetes. Not participating in regular physical activity increases the risk for obesity and type 2 diabetes but we still do not know exactly how. Within days of switching from high activity to inactivity, people have an increase in the blood sugar lowering hormone insulin but at the same time become resistant to insulin's action. This is followed by weight gain. Recent research has found that high insulin levels can cause insulin resistance and weight gain. It is possible, then, that the increased insulin level seen when becoming physically inactive causes insulin resistance and weight gain, increasing the risk of obesity and type 2 diabetes. Our study will test this hypothesis directly by using genetically modified mice that make less insulin. These mice will perform high physical activity on running wheels and then transition to low physical activity when the wheel is locked. By having a greater understanding on the mechanisms behind physical inactivity increasing the risk of obesity and type 2 diabetes, our findings could help develop treatments to prevent the onset of these diseases.
Leah Hohman	University of British Columbia	Age-related impacts of the intestinal microbiota on multiple	Progressive Multiple Sclerosis (pMS) is a prevalent neurodegenerative illness in Canada. Unfortunately, people living with pMS have limited treatment options. Age is a strong risk

Supervisor Lisa Osborne		sclerosis: defining mechanisms of neurodegeneration	factor for MS progression, indicating that biological changes that occur with age could contribute to pMS-related neurodegeneration. All forms of MS show associations with the microbiome, and the microbiome undergoes substantial changes during aging. However, whether age-related changes to the gut microbiota are important contributors to the neurodegeneration seen in pMS remains undefined. Thus, I will perform fecal microbiota transplant (FMT) of samples collected from healthy aged vs young people into microbiota-depleted mice, followed by treatment to induce a laboratory form of MS. This experimental set-up allows me to isolate the role of an aged vs young microbiota on MS outcomes. In preliminary studies, mice harbouring an aged microbiome develop pMS-like disease. I will identify specific microbes and the molecules they produce in aged FMT mice that exacerbate neurodegeneration. These studies will lead to better understanding of the mechanisms driving neurodegeneration in pMS, and the identification of new targets for this treatment-resistant disease.
Sharon Hou **Supervisor** Jennifer Coelho **Co-supervisor** Fiona Schulte	University of British Columbia	An investigation of the healthcare and psychosocial experiences of racialized youth living with serious and life threatening illnesses	We live in a diverse Canadian society that is quickly growing in social and cultural representation. A national survey conducted in Canada in 2016 estimated that children with at least one parent that was born outside of Canada is expected to make up almost half of the total population of children in Canada by 2036. With growing diversity, it is important for us to gain a full understanding of how children's social and cultural background can influence their health care experiences and identify any disadvantages or barriers some may face in their care are because of their backgrounds. The goal of this project is to better understand the health care experiences of racialized children and adolescents living with serious and life threatening illness, and to explore social and cultural reasons that may influence their understanding of and engagement in their care and well-being. This information will allow us to plan future care so that they best support the needs of youth with mental health and physical health concerns from all social and cultural backgrounds.
Stanley Hung **Supervisor** Janice Eng	University of British Columbia	An exercise- and education-based secondary prevention program after stroke: a randomized controlled trial	30% of stroke survivors will have another stroke. To prevent this, we can try to change several factors. These factors include high blood pressure (the most important factor), high blood sugar and fat levels, poor diet and mood, and smoking. Exercise can lower blood pressure, blood sugar and fat levels and improve one's mood. Lifestyle-management education can improve one's diet and mood and help stop smoking. However, we do not know if exercise and education programs can lower blood pressure and prevent another stroke in stroke survivors after rehabilitation. This study will test if an exercise and education program will lower blood pressure in stroke survivors compared to education alone. Stroke survivors recently finishing rehabilitation will be assigned by chance to one of two groups. The first group will complete an 8-week exercise and education program. The second group will only complete the education program. We anticipate that stroke survivors will have lower blood pressure after completing the exercise and education program compared to education

			alone. This will be one of the first studies in British Columbia to test if formal exercise and education programs after rehabilitation will help prevent another stroke.
Michael Hunter **Supervisor** Carolina Tropini	University of British Columbia	Leveraging phage infection to decrease pathobiont virulence in inflammatory bowel disease	The makeup of bacterial communities in the gut is strongly linked with inflammatory bowel disease (IBD) including Crohn's disease and ulcerative colitis. Pathobionts like E. coli are opportunistic pathogens that exacerbate gut inflammation in IBD but respond poorly to antibiotics. Bacteriophages (phages) – highly specific bacterial viruses – can alter gut microbiome composition, and so could be used in IBD treatments. Phages, however, undergo evolution – they change over time in response to their environment. Their safe and effective use in treatments therefore requires an understanding of how they co-evolve with the pathobionts in the gut. Here, I will study E. coli pathobiont and phage co-evolution in the gut in response to malabsorption – a key symptom of IBD that causes high gut osmolality (concentration of molecules). Bacteria can adapt to these changes by regulating osmotic channels, but at a cost: phages use those channels to infect. By combining a computational model of bacteria-phage growth with evolution experiments performed in the gut, I will determine the role played by malabsorption in driving bacteria-phage co-evolution and reducing pathobiont load, in turn informing the development of phage therapies for IBD.
Haifeng Ji **Supervisor** Kizhakkedathu Jayachandran	University of British Columbia	Prevention of biomaterial-induced thrombogenesis without interference of coagulation system by modulating the protein activity on material-blood interface	When the blood-contacting materials are applied for specific applications such as hemodialysis and blood transportation, our body will regard them as an "invader", and quickly activate the coagulation system to "protect" itself. The activation of coagulation will induce thrombosis, resulting in early treatment termination or lead to other complications such as pulmonary embolism. In clinical practice, the use of anticoagulants to temporarily block the coagulation system to perform such medical procedures, however, significant challenge arises as normal hemostasis is impaired in anticoagulant action. Many patients treated with anticoagulants have to be repeatedly hospitalized due to life-threatening bleeding. In fact, there is no material currently available which is truly antithrombotic. Building on a new concept, in this project, we will focus on developing a universal surface modification approach that can be applied to any device to avoid the surface-induced thrombus generation without interfering the normal hemostasis. The benefits of this research are immeasurable, nearly 2.6 million patients worldwide will be benefited from it annually in the field of hemodialysis alone, not to mention the other areas mentioned above.
Verónica Jiménez Sábado **Supervisor** Glen Tibbits	Simon Fraser University	Facilitating clinical use of single nucleotide polymorphisms associated with atrial fibrillation by linking them to molecular signaling pathways and electrophysiological dysfunction.	Atrial fibrillation (AF) is the most common cardiac arrhythmia affecting more than 35 million people worldwide. It is an age-dependent progressive disease that doubles mortality, degrades life-quality, and becomes increasingly difficult to treat with time. Therefore, it is essential to find new biological markers that allow early identification of individuals prone to develop AF and to optimize the treatment of the arrhythmia. Recently more than 100 genetic markers which are referred to as single nucleotide polymorphisms (SNPs) have each been

			associated with a modest increase in the risk of developing AF. Since all of us have several of these risk SNPs, the challenge, in which this project aims to engage, is to identify combinations of SNPs that confer a high risk of AF and discover how they affect the function of the heart cells. This will then allow health professionals to use SNP analysis to improve risk prediction and to personalize the treatment of people with AF according to the risk SNPs they carry.
Bradley Jones **Supervisor** Caroline Colijn	Simon Fraser University	Novel Bayesian phylogenetic methods for understanding HIV evolution within and between host	Human immunodeficiency virus (HIV) the cause of AIDS continues to affect 40 million people worldwide. To tackle the HIV pandemic, we need to develop sophisticated tools that will increase our understanding of HIV. I plan to develop new tools for understanding HIV combining phylogenetic trees and Bayesian methods. A phylogenetic tree records the ancestral relationships of viruses, like a family tree of viruses. Bayesian methods are advanced statistical techniques that achieve more accurate results over traditional methods. First, I will create better tools for making diagrams of phylogenetic trees with computer software. These diagrams will make it easier for scientists to present their findings and interpret others' results. Second, I will develop a Bayesian method to characterize the spread of HIV while protecting individuals' identities. This will facilitate targeted intervention to stifle HIV transmission within the community. Finally, I will compare the effectiveness of different techniques to determine the make up of the infecting virus of an individual living with HIV by looking at the characteristics of their HIV. Overall, my new methods will help complete our understanding of HIV and bring an end to the HIV pandemic.
Shahin Kassam **Supervisor** Victoria Bungay	University of British Columbia	Women and Forced Migration: Inclusively Examining Access to Care at the Axes of Chronic Health and Gender-Based Violence	Forced migration occurs when people are displaced from their homes to escape harmful situations including human rights violations, and/or environmental disasters. Currently, over 40 million women and girls have been forced to migrate worldwide. Most have been racially discriminated and over 70% have been exposed to gender-based violence (GBV) including human and sex trafficking, exploitation, and forced marriage. Health impacts of GBV include chronic health issues including hypertension, diabetes, and post-traumatic stress syndrome. Canada's population of women forced to migrate is steadily growing. However, access to timely and appropriate health services remains uncoordinated and ineffective. Upon arrival to Canada, women are left to self-navigate exclusionary and fragmented pathways to health care while also managing the effects of forced migration. In this research, the experiences of these women will be gathered and examined toward generating recommendations for enhanced access to safe and effective health care. This project responds to national and global calls to address a significant gap in knowing how to deliver timely and safe care to women impacted by forced migration and managing the chronic health sequelae of GBV.

Seongho Kim **Supervisor** Isaac Li	University of British Columbia	Harnessing NK cell mechanics for fine-tuning cancer immunotherapy	Cells of the immune system help maintain health and defence against cancer by detecting and killing cancer cells in the human body. Immunotherapy is a cancer treatment strategy that boosts the immune system to fight cancer using native immune cells made in the body. Natural killer (NK) cells are a subpopulation of immune cells. NK cell-based immunotherapy has gained attention for cancer treatment due to the relatively simple procedure, although their low efficacy remains a challenge, despite many breakthroughs. An NK cell has a sophisticated molecular architecture that dynamically changes when interacting with neighbouring and target cells. When NK cells encounter cancer cells, their molecular architecture is changed to enhance their ability to combat cancer. However, details of how this happens are not entirely understood, limiting our ability to engineer them for fighting cancer. I will study the properties of cellular structures under the stimuli of weak or strong immune responses to find the best cellular architecture for cancer immunotherapy. An understanding of structural change during immune response will provide valuable information to devise a novel strategy for cancer treatment.
Linda Lapp **Supervisor** Scott Tebbutt	University of British Columbia	Identification of biomarker signatures predicting short- and long-term complications following heart transplant surgery	Patients have heart transplant surgery as a life-saving measure after heart failure, and it is crucial to minimize unwanted postoperative outcomes. One of the major negative outcomes following heart transplant surgery is acute rejection, which is currently managed with strong immunosuppression treatment. However, this treatment can lead to other unwanted side effects, such as kidney problems and cancer, experienced by 50% and 30% of patients, respectively. To address this problem, I will analyze biomarkers, or biological molecules found in the blood that can be measured to indicate the various negative outcomes after heart transplantation. Our research group has measured biomarkers in blood extensively and to build on that work, I will use statistical and machine learning analysis techniques to find the biomarkers that could predict and potentially diagnose complications after heart transplant surgery. Achieving this goal will help develop personalized immunosuppression treatments for patients to reduce adverse health outcomes and improve overall patient care after heart transplantation.
Anthony Lapsansky **Supervisor** Douglas Altshuler	University of British Columbia Partner: Parkinson Society BC	Coordinating movement in a complex world: How the midbrain and oculomotor cerebellum encode visual motion originating from realistic scenes to guide locomotion	As we move about the world, we experience optic flow - the movement of surfaces and objects resulting from self-motion. Studies of human behaviour have shown that optic flow is critical for controlling posture, walking, driving, and navigating complex environments. Deficits in optic flow processing are linked to diseases including vertigo, oscillopsia, ataxias, Parkinson's disease, and Alzheimer's disease. Determining how and where the brain processes optic flow is therefore crucial to human health and behaviour, but major gaps in knowledge remain. Typically, optic flow processing is studied by exposing subjects to simple patterns. These methods allow for tight control of experimental designs, but simple patterns lack features provided by the real world – features we use every day. How and where the brain encodes realistic visual motion to control our movement is almost entirely unknown.

			This severely limits our ability to treat those with optic flow deficits. This proposal aims to understand how and where the brain processes visual motion originating from realistic scenes using pigeons as a model system.
Clarus Leung **Supervisor** Don Sin	University of British Columbia	Endo-phenotyping of Asthma and Chronic Obstructive Pulmonary Disease Overlap by Airway Inflammation and Structure	Chronic obstructive pulmonary disease (COPD) and asthma are two different diseases that affect the airways. Around one-third of COPD and asthma patients have features of both asthma and COPD and thus are diagnostically labeled as asthma-COPD overlap (ACO). ACO patients experience worse symptoms and more serious respiratory attacks than those with COPD or asthma alone, but we do not know why. To address these questions, our study will investigate the underlying inflammatory mechanisms in the airways of patients with ACO. We will collect tissue samples and cells from the airways of volunteers with ACO using a technique called bronchoscopy and perform genomics on these samples. These data will enable us to identify the key airway features of ACO. We will also use this cohort to determine which features of ACO lead to a good therapeutic response from inhaled corticosteroids, a class of medications used in COPD and asthma. We will use high-resolution imaging techniques to investigate how inflammation relates to persistent changes in the structure of the airways and the lungs. Our research will reveal the disease mechanisms of ACO so that we can better diagnose and prescribe the most effective therapies for ACO in clinical practice.
Samara Mayer **Supervisor** Marilou Gagnon **Co-supervisor** Kelli Stajduhar	University of Victoria	Characterizing the pain needs of structurally vulnerable palliative care patients with substance use disorder	An important part of palliative care is managing pain, including physical, emotional, mental and spiritual suffering. However, people with substance use disorder (SUD), who experience homelessness and poverty (for example), face barriers in having their pain needs met. These unmet needs are due to gaps between palliative and substance use care, and because this group of people face social and health care barriers that limit their access to resources and support. Unmanaged pain among this group can have significant consequences, including suffering at the end of life and increasing risk of negative health outcomes, such as overdose. This study will examine the pain needs of palliative patients with SUD, gaps in the management of pain for this population and develop approaches to meet these needs. Research activities include interviews with palliative care patients with SUD and service providers, observations in care settings, and mapping tools to understand the broader scope of the topic. By making connections between pain management approaches among palliative and substance use health care, this research will generate new ideas to improve the management of pain among palliative care patients with SUD.
Andrea Mellor	University of Victoria	Strengthening safety nets to improve access to substance use and mental health services	Despite an increasing trend in the number of youth with substance use disorders in BC, current data shows that voluntary, community-based, and youth-friendly support services are lacking. My project aims to address this gap by learning from youth who have had their lives impacted by substance use. By engaging with youth as co-researchers in this project, I will

Supervisor Cecilia Benoit		to optimize youth-determined health and wellness	better understand their diverse hopes, wishes and ideas for accessible, non-judgmental, and culturally centered substance use and mental health services. First, I will establish a leadership circle that engages a diverse group of Indigenous, non-Indigenous, immigrant and refugee, 2SLGBTQIA+, and pregnant/parenting youth, who receive(d) services from our local partners, the Foundry Victoria Youth Clinic Society (VYCS) and Surrounded by Cedars Child and Family Services. We will co-create a shared vision for meaningful and accessible substance use and mental health services, grounded in each person's own experience and recommendations. This vision will be translated into an intervention to pilot, implement, and evaluate at Foundry VYCS and inform later implementation with the Foundry Network in British Columbia.
Brian Mooney **Supervisor** Gregg Morin **Co-supervisor** Poul Sorensen	BC Cancer	Developing TMEM119 as an attractive immunotherapeutic target in Osteosarcoma	With current treatment options, patients with Osteosarcoma have a 5-year survival rate of about 76%, but for 3 out of 4 patients diagnosed with Osteosarcoma that has spread beyond the primary site will not live 5 years passed their diagnosis. There is clearly an unmet clinical need to develop new options for these patients. Immunotherapy aims to notify your body of the malignant cells and target them for destruction by the patient's own immune system, however, its success in pediatric cancers is still lacking. One crucial aspect of developing successful immunotherapies is having a good target, and these are often targets that sit on the outside surface of the cancer cells. Our team has already characterized this area in Osteosarcoma and found a protein, TMEM119, to be extremely specific to Osteosarcoma. We have demonstrated that TMEM119 is not expressed in normal tissues, only in some sarcomas, making it an ideal strategy to target, but more work is needed. With this project, we aim to understand the role of TMEM119 in Osteosarcoma by selectively switching it off and examining whether this can prevent the spread of Osteosarcoma. We hope that our work can contribute to the development of a new strategy for Osteosarcoma patients.
Francis Mwimanzi **Supervisor** Mark A. Brockman **Co-supervisor** Zabrina L. Brumme	Simon Fraser University	Leveraging longitudinal COVID-19 vaccine cohorts to deconstruct SARS-CoV-2-specific adaptive immune responses and the potential for viral infection to induce immune amnesia	Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in >400 million documented infections and ~6 million deaths worldwide. Safe and effective vaccines have significantly reduced morbidity and mortality due to COVID-19, but even the newest bivalent vaccines provide only limited protection against infection with current SARS-CoV-2 variants. Further in-depth analyses of immune responses to COVID-19 vaccines and SARS-CoV-2 infection are needed. Moreover, the rise in non-COVID-19 respiratory infections in 2022 has led to speculation that SARS-CoV-2 may impair immune responses to other pathogens. This is plausible since SARS-CoV-2 can dysregulate B cells, the specialized immune cells that produce antibodies, but few studies have examined this. My research will examine the generation of B cell responses against the original (ancestral) SARS-CoV-2 and newer Omicron variants in a diverse cohort of vaccinated adults. I will characterize B cells that cross-react with ancestral and variant

			Spike, which are likely to help protect against new strains. Finally, I will explore the consequences of SARS-CoV-2 infection on B cell responses to other respiratory viruses.
Elizabeth Nethery **Supervisor** Laura Schummers **Co-supervisor** Kimberlyn McGrail	University of British Columbia Partner: BC Children's Hospital Research Institute	Team-based postpartum and infant care models: effects on service use, outcomes, and health system costs in the one year after birth	The months following childbirth may be difficult for new parents caring for a new baby (or babies) while recovering from pregnancy and birth. Team-based maternity care draws on the strengths of interprofessional teams (physicians, midwives and allied health) to improve patient care and outcomes and is a current provincial priority in British Columbia (BC). Midwifery care provides frequent post-delivery contacts, at-home care, and on-call support during this critical postpartum period. There is a growing trend in BC towards informal team-based arrangements where midwives support mother-infant dyads after physician-attended birth. In other settings, up to 18% of postpartum individuals and 8% of newborns visited the emergency department in the postpartum 6-week period. We will examine whether interprofessional team-based partnerships in which midwives provide postpartum care is associated with hospital service use (emergency department visits, hospital readmissions), maternal or infant outcomes, and health system costs in British Columbia. Findings will inform knowledge users in health policy and system leadership positions by evaluating this aspect of team-based maternity care applied in the postpartum period.
Michelle Ng **Supervisor** Marco Marra	University of British Columbia	Effect of HPV integration on 3D genome structure and function in cervical cancer	In human cells, DNA is folded such that distant points on the linear genome may lie close together in 3D space. This allows interactions between some regions of DNA while separating others, thus dictating the connections between genes and regulatory elements, and exerting control over gene activity. When 3D genome organization is disrupted, the wiring of genes and regulatory elements can be altered and lead to aberrant interactions that inappropriately activate pro-cancer programs. Viral infections cause 10% of cancers, of which 50% are attributable to human papillomaviruses (HPV). Cervical cancer is a HPV-driven disease, and in over 80% of cases, viral DNA becomes inserted ("integrated") into the DNA of infected cells, leading to genome disruption. I will profile DNA folding in cervical cancer cells to investigate how HPV integration disrupts the organization and regulation of the host genome, and how this dysregulation contributes to cancer. My study will contribute to understanding the role of HPV integration in cervical cancer. Findings in this context may improve our understanding of genome dysregulation in other HPV-associated cancers, and provide general insights into how viral integration can promote cancer progression.
Amanda Orr	University of Victoria	3D bioprinting patient-derived neural tissues for screening	Alzheimer's disease (AD) is the most common form of dementia and continues to affect more people globally due to the aging population. AD currently has no treatment or prevention

Supervisor Stephanie Willerth	Partner: CLEAR Foundation	potential treatments for Alzheimer's disease	options aside from symptom alleviation, making it a high priority in medical research. Despite years of research, no AD treatments have been discovered since most studies have used tissue replicas (or models) that do not accurately act like the brain. This has led to presumed success of treatments in research, but failure in clinical testing in animal models. The use of three-dimensional (3D) models that contain brain cells organized in a more accurate 3D structure will allow for a better understanding of AD, which is the focus of this work. In addition, these 3D models can include patient cells to provide specific treatment options for those with AD. The patient-specific AD models will be used to test various drugs, including those with current approval for other diseases. The proposed research will provide new insight into AD treatments by using more accurate AD models to better understand this complex disease in research. The 3D tissue models will allow for better screening of treatment options, ultimately bringing us closer to finding a cure for AD.
Yihang Pan **Supervisor** Michael Gordon	University of British Columbia	Mosquito taste receptors for detecting human sweat and initiating blood feeding	The World Health Organization estimates around 725,000 mosquito related deaths a year. This makes mosquitoes one of the deadliest animals on Earth. Mosquitoes bite us humans to get nutrients and pass deadly diseases to us as a consequence. It is well studied that mosquitoes rely on their sense of smell to find us. Yet, what triggers them to bite us once they land on our skin is unknown. We hypothesize that mosquitoes use their sense of taste to trigger the biting behaviour. In addition, taste receptors on their legs play a crucial role in triggering biting. We will test this by first identifying which receptors will respond to human sweat. This will be done by presenting individual receptors with human sweat and identifying the ones that respond. We will then follow up by removing these receptors from the legs of mosquitoes to see if they will still bite. This will allow us to find the receptors that trigger the biting behaviour in mosquitoes. With this information, we can find safe compounds to deter mosquito biting. We can also design mosquitoes that are bad at biting to be released into the wild to produce offspring that are bad at biting as well. A combination of these methods can protect us from mosquito diseases.
Amber Paulson **Supervisor** Jeffrey Joy	University of British Columbia	Combatting infectious diseases through understanding epigenetic interference – A case study: SARS-CoV-2	Severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) has caused 6.5 M deaths globally. Despite currently available vaccines and treatments, we need more effective therapeutics to combat the ongoing SARS-CoV-2 pandemic which remains a major global health and economic challenge. RNAaemia (a high level of viral RNA in the blood) is a predictor of poor health outcomes in COVID-19. Therefore, the MOD-RNA pipeline was developed to analyze RNA produced by SARS-CoV-2, but in a manner consistent with the principle that RNA is the epicenter of genetic information. My research reveals SARS-CoV-2 produces small RNAs with an affinity for human genome enhancer regions. These findings support that SARS-CoV-2 has evolved epigenetic interference to promote viral propagation by abrogating transcriptional networks critical to the infection process. To facilitate ongoing surveillance of SARS-CoV-2 variants of

			concern, I plan to continue building out MOD-RNA as an open-access tool, which will also be broadly applicable to other current and emerging pathogens. This research and further development of MOD-RNA is critical to our fight against SARS-CoV-2 because of the potential to find new therapeutic opportunities against COVID-19.
Athena Phoa **Supervisor** Xiaoyan Jiang	BC Cancer	Restoration of miR-185 in combination with BCR-ABL downregulation by non-viral delivery of siRNA with lipomeric carriers and lipid nanoparticles sensitizes drug resistant cells to TKIs	Over 130,000 people in Canada are living with and are actively being treated for blood cancers. The main problem with our available current therapy is their inability to kill blood cancer stem cells that are responsible for drug resistance and cancer relapse. Our lab has found that targeting a novel pathway using gene therapy to restore the activity of miR-185 can significantly impair the growth of blood cancer stem cells and sensitize them to therapy. This study will investigate the combination of targeting several key proteins using miR-185 and targeting BCR-ABL using siRNA in order to effectively eradicate blood cancer stem cells. Importantly this treatment strategy does not show any side effects in normal blood stem cells, providing a therapeutic window to specifically target blood cancer stem cells. This study aims to investigate the therapeutic potential of this gene combination using gold-standard lipid nanoparticle technology and a newly established animal cancer model. We hope this work will provide a proof-of-concept for more effective strategies to overcome drug resistance and improve the outcomes of patients diagnosed with blood cancers.
Sruthi Purushothaman **Supervisor** Freda Miller	University of British Columbia	Understanding the cellular and molecular mechanisms of fingertip (digit tip) regeneration in mammals	Approximately two million people in North America are living with lower limb loss, caused predominantly from complications of diabetes, peripheral vascular disease, trauma and cancer. The ability to regenerate an organ varies widely across the animal kingdom; while amphibians can regenerate entire limbs, mammals have largely lost this ability. One exception to this rule is the tip of the finger (or digit tip in mice, the model system studied here). In mammals including humans, the fingertip will regenerate completely and appropriately as long as the base of the nail (or nail bed) is still intact or else lead to scar formation. In this proposal, we will study adult mice to ask why this one small part of the body has retained the capacity to regenerate and what controls the decision to regenerate or to form a scar. Similarities with human fingertip injury responses make our system one of the most clinically relevant models of tissue regeneration in a mammal. My proposed study will explore how the nail bed creates an environment enabling regeneration rather than scar formation, and will identify the soluble signals from the nail bed that communicate with other stem cells that ensures the generation of a new fingertip.
Castel Ramirez **Supervisor** Pamela Hoodless	University of British Columbia	Defining epigenetic alterations in liver cancer at single cell resolution	Hepatocellular carcinoma (HCC) is the most common liver cancer and is predicted to become the third most prevalent cause of cancer mortality by 2030. Therapeutic options are limited and those that are available have inadequate efficacy. HCC tumors share similarities with developing liver cells and express genes important for liver development. However, the genetic basis of these similarities still remains unclear. Many liver cancers have mutations in

			genes that regulate chromatin structure, however how chromatin is altered in HCC and how this contributes to abnormal gene expression have yet to be examined. Our study will utilize advanced single-cell genomic methods to identify changes in chromatin structure in HCC tumors and compare them to adjacent liver tissue and normal livers. This will lead to the identification regulatory DNA sequences and their gene targets associated with HCC progression. We will investigate the function of these DNA sequences and their gene targets in the context liver development using a model of human liver development derived from stem cells. Our study will result in a better understand the molecular underpinnings driving HCC and facilitate discovery of improved therapeutic targets.
Md Mohosin Rana **Supervisor** Jayachandran Kizhakkedathu	University of British Columbia	Enhancing Immunomodulation by Novel Glycoconjugate-Based Organ Engineering to Prevent Transplant Rejection	Organ transplantation is a lifesaving therapy. In 2021, in Canada around 2,782 organ transplants were performed. Key to success in organ transplantation is to suppress the immune system and prevent rejection. Current treatment using immunosuppressive drugs have reduced the incidents of rejection, however, such global immunosuppression leads to severe side effects. Thus, new approaches are needed for improved graft survival. Graft rejection is a comprehensive immune reaction initiated due to the damage of blood vessel lining (glycocalyx) during organ procurement and preservation. Such damage mediates the migration of a variety of immune cells post-transplantation, and worsen overtime triggering rejection. In this project, we will rebuild native immune-deactivating activity using immunosuppressive polymer conjugates via a novel organ engineering approach to prevent such damage and graft rejection. We will study the mechanism of this approach and apply it in the transplantation of arteries and kidneys as proof-of-concept. This new organ engineering will reduce the post-transplantation treatment costs, improve patients' quality of life and may lead to transplantation without immunosuppressive drugs.
Marta Ruiz Alguero **Supervisor** Helen Tremlett	University of British Columbia Partner: Tai Hung Fai Charitable Foundation with Edwin S.H. Leong Centre for Healthy Aging Program	Advancing understanding of the multiple sclerosis (MS) prodrome: a focus on understudied signs and symptoms (MS-Pro-Us)	Multiple sclerosis likely begins years before the first neurological symptom. During this period, it can present as a set of yet to be well-defined, subtle symptoms, leading patients to increasingly seek medical attention years before actual MS symptom onset, and diagnosis. Our aim is to better understand the earliest signs of MS. We will look for poorly understood signs and symptoms such as sleep disturbances, palpitations, shortness of breath, and skin conditions among others that may appear months or years before MS onset. We will see if these signs are different in men and women and how such differences vary across different age groups. In addition, previous studies suggested that women who developed MS had fewer pregnancies and increased contraceptive use in the five years before MS onset. This may reflect lifestyle changes even before MS onset. We will look at all these issues in more depth than has ever been done before. We will have access to health data from large populations so that we can look in detail at people with and without MS. Our aim is to help doctors and researchers recognize when MS actually starts and to help doctors, patients and families get prompt, appropriate treatment for everyone who develops MS.

Paulina Scheuren **Supervisor** John Kramer	University of British Columbia	Spinal cord temperature as a measure of neuroinflammation in the human spinal cord	The lack of effective treatment options for neurological disorders underlines the critical need to identify new drug targets. Neuroinflammation is one of the most common disease mechanisms in various neurological disorders, which makes it a promising target for novel therapies. One of the major barriers facing the development of effective therapies that improve function in individuals with neurological disorders, such as spinal cord injury and multiple sclerosis, is the lack of suitable biomarkers. To address this issue, we aim to develop "spinal cord thermometry" or SCT. SCT can be done in awake individuals using data acquired from a non-invasive MRI scan. SCT, we believe, may provide valuable information on the degree of inflammation ongoing in the injured spinal cord. This is, conceptually, very similar to how body temperature indicates if you have an infection. Our study will develop the necessary methods to measure SCT, first in healthy individuals, before application in individuals with spinal cord injury and multiple sclerosis. Our research will provide a novel biomarker of neuroinflammation in the spinal cord and help identify ways to treat diseases associated with neuroinflammation.
Glen Lester Sequiera **Supervisor** Mahmoud Pouladi **Co-supervisor** Michael Hayden	University of British Columbia	Investigating the mechanisms underlying abnormalities in neuronal activity through human pluripotent stem cell-derived microglia-sufficient brain organoids in Huntington's disease	Microglia are the immune defense cells located within the brain and also play a big role in the maintenance of a healthy brain by scavenging and removal of damaged/unnecessary neurons and synapses. This "synaptic pruning" function is important for the proper developmental wiring of the brain. Huntington's disease is a disorder of the brain, which gets worse over time. It is caused by DNA repeat expansions in Huntingtin gene leading to neuron cell toxicity and death. Of late, the role of microglia in Huntington disease development has been gaining momentum. I plan to study the effects that different DNA repeat sizes in Huntingtin gene have on the disease progression, through the repeats' influence on the microglia's behaviour and function as well as on the neurons' reaction to synaptic pruning. Further, I will check if correcting either microglia/neurons or both would be useful in reducing the cellular symptoms of Huntington's. The results will throw light on early development changes (influenced by different sizes of DNA repeats) that would occur in Huntington's disease and also reveal how they impact a disease like Huntington's, which usually affects patients late in their life.
Kristina Smith **Supervisor** Kelli Stajduhar	University of Victoria	Exploring oncology care providers' treatment decision making and its impacts on individuals who are highly marginalized with cancer	Due to racism, discrimination, stigma, mental illness and substance use issues, and homelessness, highly marginalized adults tend to die alone, in pain, with their needs unmet, and sometimes of preventable and treatable cancers. Cancer is the leading cause of death for highly marginalized adults. Oncology care providers play a critical role in providing culturally safe, effective care that aligns with individuals' needs, but, issues such as unstable housing, transportation barriers, mental health and substance use issues can create conditions where oncology care providers are placed in a position of making treatment decisions that are challenging because, if highly marginalized adults do come to the cancer clinic, their treatments often dictate a regimen that is difficult to follow. This study will explore

			the factors that oncology care providers consider when making decisions about cancer care treatments for highly marginalized adults. Results will inform the development of clinical practice guidelines to support oncology care providers' decision-making when making treatment decisions for adults who are highly marginalized.
Sian Tsuei **Supervisor** Lindsay Hedden	Simon Fraser University	Investigating telemedicine's impact on technical quality of care	Telemedicine became an integral part of health services delivery during the COVID pandemic for Canada and will likely remain so thereafter due to potential for improving access and patient satisfaction. However, telemedicine likely has its limits. Telemedicine may not be suitable for all cases. Telemedicine can mainly provide visual and verbal information, and some medical conditions and complaints require additional forms of information. Using telemedicine for inappropriate medical conditions or complaints may undermine the technical quality of care. Drawing on administrative data, this project seeks to examine the kinds of medical conditions and complaints associated with worse quality of care on telemedicine, if continuity of care mitigates such adverse impact, and if such negative impact is distributed inequitably. The findings has implications for policymakers, health care organization leaders, providers, and medical educators regarding how to best adjust the relevant policies and practices so that telemedicine can be used most appropriately.
Marie Yan **Supervisor** James Johnston **Co-supervisor** Theodore Marras	University of British Columbia	Population-Based Analysis of Nontuberculous Mycobacterial Pulmonary Disease in British Columbia	Nontuberculous mycobacteria (NTM) are a group of environmental bacteria, commonly found in water and soil. Many species of NTM – such as Mycobacterium avium complex – can cause chronic lung infections, which are difficult to treat and often associated with progressive lung damage. The number of people affected by NTM lung disease has been increasing around the world, however, we do not have a good understanding of its local impact. In this project, we will use province-wide data to characterize the scope of NTM lung disease in British Columbia (BC) and examine treatment patterns. We will also assess challenges associated with treatment, including early treatment discontinuation and bacterial resistance to antibiotics. Findings from this study will improve our understanding of the patient population affected by NTM lung disease in BC and inform efforts to improve the care of these patients.