Faculty of Medicine Multidisciplinary Research Program in Medicine Evaluation Report

2021 Summer Pilot Program

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for Faculty of Medicine Office of Research

THE UNIVERSITY OF BRITISH COLUMBIA

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Program Overview

Program Description

The Faculty of Medicine Multidisciplinary Research Program in Medicine (FoM MRPM) was designed to provide undergraduate students with an opportunity to explore their interest in interdisciplinary and multidisciplinary research by undertaking a summer project supervised by a cross-faculty pair of researchers. We designed this pilot project with the goal to assess program enrollment and delivery based on the success of the University of British Columbia at Okanagan's Multidisciplinary Undergraduate Research Projects in Health (MURPH) program. The current document is an evaluation of this pilot program with the intention to modify and improve the program in order to expand it's reach in future years.

"I was hoping to be closely involved on an independent project where I could actively pursue potential answers to a research question. The project exceeded my expectations in not only providing me with the opportunity to do so, but also in enabling do everything in an extremely positive work environment with an amazing team."

-Student Awardee

The goal of the program was to pair researchers across faculties with undergraduate and MD students for the purposes of conducting multidisciplinary/interdisciplinary research. With this goal in mind, successful primary supervisors from the Faculty of Medicine (FoM) and co-supervisors from across UBC were matched with two non-MD undergraduate students and were given the option of one MD student for their research project (see Figure 1 for co-supervisor disciplines). Undergraduate and MD students conducted 16- or 8-weeks of full-time research, respectively. A Postgraduate Student Advisor was assigned by the supervisors to spearhead training and oversight on the project and gain valuable supervisory experience.

Objectives

The FoM MRPM aimed to provide unique funding opportunity for researchers to collaborate across disciplines, in-line with overall FoM strategic plan, and to provide training and professional development to UBC undergraduate students. Specifically, these student learning objectives included:
- Networking and collaborating with supervisors and students across typically siloed disciplines
- Fostering scientific communication skills including opportunities to give a research conference presentation
- Developing concrete research skills that will have a meaningful impact on future student success and further important research goals

Approach

Application Process

"FoM MRPM was very well organized and facilitated faculty to find talented junior students to train and help with our research activities."

"Great support for students and connecting them with researchers who sometimes have hard time connecting to excellent undergraduate students"

-Primary FoM Supervisors

Separate application portals were open for supervisors and students on February 1st, 2021 and closed on March 15th, 2021. Supervisor applications required a FoM-appointed primary supervisor to collaborate with a non-FoM co-supervisor and choose a postgraduate student advisor to help supervise the project. Along with contact details, supervisors were required to write a project summary and benefit to the student statement for review. These statements were packaged and sent for adjudication to a panel of researchers to score (see Table 1 for adjudicator scoresheet). Students accessed a separate application portal where they entered their contact details as well as a student statement as to why they wanted to be considered for this program. Eleven project applications were considered, with ten projects selected for funding based on a previously agreed upon funding allotment (the eleventh project was not eligible as it was not multidisciplinary or interdisciplinary in nature). Successful project supervisors were notified and given an anonymized list of eligible students (and their student statements) to interview. For one project, supervisors had students in mind and so were assigned these students after an eligibility check. Most supervisors rank ordered their top five students from the list and were assigned students based on all other rankings.

Criterion	Points	Notes
Project Summary The project must be based on a clear and testable research question(s) or hypothesis. Projects not meeting this requirement are not eligible for the FoM MRPM.	**60 points**	This section should address the scientific merit and feasibility of the proposed project. Considerations when scoring this section include:
		• Clear interdisciplinary/multidisciplinary focus
		• Clear rationale for the proposed research approach and methodology, including the context within the relevant field of research.
		• Clear and testable research question or hypothesis.
		• Feasibility of the research approach including the project timeline.
		• Expected project outcomes.
Benefit to the Student Students should benefit from their involvement and come	**40 points**	This section must address how involvement in this project will help the student gain an understanding of how high-quality research is conducted. This includes addressing the opportunities to learn new skills (or develop existing skills) in the context of the following learning objectives (**as applicable – not all will be applicable to all projects**). As a result of their FoM MRPM experience the student will gain an understanding of:

away with new knowledge, new skills, and a better understanding of what interdisciplinary/multidisciplinary research entails.		• How to generate testable research questions and/or hypotheses
		• How to critically evaluate & analyze existing literature/data
		• The principles of experimental design
		• The ethical principles of research
		• How to critically analyze data; appropriate statistical analyses
		• Effective scientific communication (such as presentations, manuscripts, guidelines, patient learning materials, etc.)
		• Specific techniques/skills required for the project (of lesser importance in scoring than the above learning objectives)
		Additional considerations when scoring this section:
		• The student's learning objectives and role are clearly defined.
		• The fulfillment of additional learning objectives (not discussed above) related to the conduct of medical research.
		• Student has the opportunity to interact with and learn from other researchers (will help the student gain a broader understanding of what research entails).
		• The project has strong research and educational merit.
		• The project can be completed in the time available.

Table 1. Adjudicator scoresheet.

Program Interest

Interest in the program was high given the short timeframe between launch and implementation. We launched February 1st, 2021, advertising the program widely throughout UBC. Applications were due March 15th, 2021, giving applicants only 6-weeks to submit applications for a new cross-disciplinary program that required collaboration between faculties.

Research Project Applications	Student Applications
11	113
Funded Research Projects	**Student Awardees**
10	24

Table 2. Total number of project and student applications and funded awardees for the 2021 MRPM Pilot Project Research Projects

Supervisors

A total of 10 FoM supervisors and 10 non-FoM co-supervisors were a part of the FoM MRPM. Primary supervisors were required to hold a FoM appointment. Co-supervisors were required to hold appointments outside of the FoM. There were no restrictions on the co-supervisor's Faculty or Department except that they could not be primarily appointed by the FoM. The only exception was that co-supervisors could be appointed through the School of Biomedical Engineering. This was to encourage collaborations across faculties and departments and facilitate multidisciplinary/interdisciplinary research. These co-supervisors were from the School of Kinesiology, Department of Microbiology and Immunology, Department of Electrical and Computer Engineering, etc. (see Figure 1 for full list of co-supervisor disciplines).
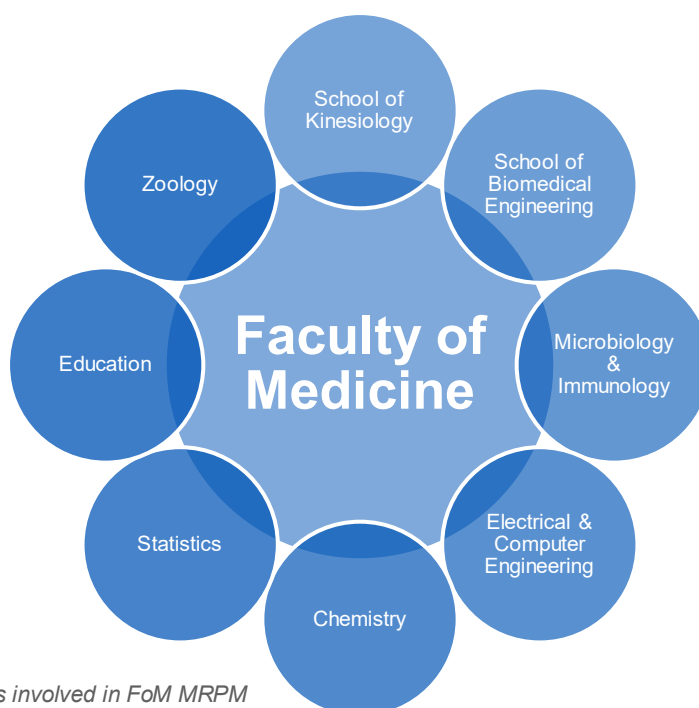
Figure 1. Disciplines involved in FoM MRPM

"Amazing students. Thankful for the funding and the program to have allowed us to recruit them. I would have not been able to take them if it weren't for this program. I hope to have impacted their careers as well. One of them will want to stay with the lab for Masters degree, and both will stay for this academia year continuing as undergraduate research students."

-Primary FoM Supervisor

Undergraduate Students

A total of 24 students were appointed to the FoM MRPM program for summer 2021. Two upper year non-MD undergraduates (years 2-4 of their program) were assigned to each of the ten funded research projects and one first-year MD student was assigned to four research projects (based on supervisor interest; see Figure 2A for program breakdown). Demographic information on these students is limited to their self-reported gender, with 15 females and 9 males awarded through this program (see Figure 2B).
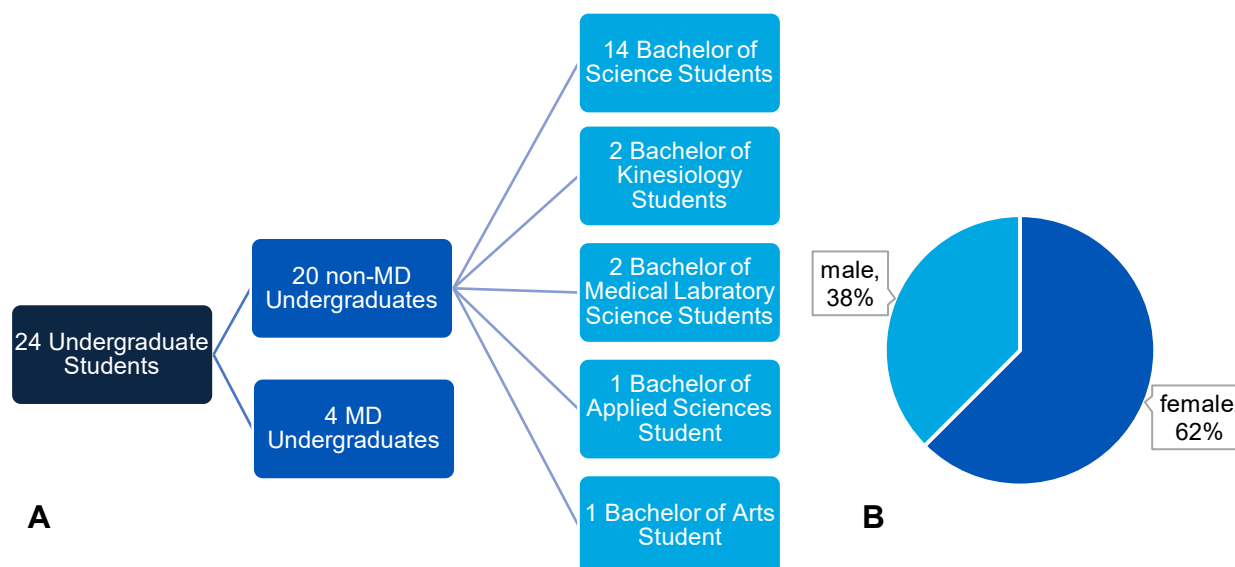
Figure 2. A) Number and program of student awardees. B) Gender demographic information on student awardees

Funding

Funding was provided for research projects in the form of student stipends. Non-MD Undergraduates received at least $8,312.60 for 16-weeks of full-time research, an amount equal to the NSERC Undergraduate Student Research Award (USRA). Of this total, $6,000 was provided by the FoM with supervisors contributing at least $2,312.60. MD students received $3,200, all of which was provided by the FoM, equal to the FoM Summer Student Research Program (SSRP). The total funding amount for this program was ~$181 000 (see Table 3 for breakdown). Funding was derived from a combination of FoM Endowments typically allocated to the FoM SSRP and supervisor contributions.

"We're just grateful that people like you are promoting creativity in science and providing real opportunities for students to gain research skills. These training initiatives will have numerous short-term and long-term benefits to the people involved in the research as well as is the eventual aim, the general public and community health."

-Primary FoM Supervisor

Total Program Funding	Total Internal Funding	Total Supervisor Contributions
$181,226.80	$132,800.00	$48,426.80

Table 3. Funding breakdown for the 2021 MRPM Pilot Project

Workshops

Workshop Overview

Workshop 1

The theme of this workshop was research design. During this workshop we had speakers present on both quantitative and qualitive methods of research design. Dr. Biljana Stojkova from Applied Statistics and Data Science

(ASDa) Group provided a 2-hour research design presentation for students to watch on their own time prior to the workshop. During the workshop students could ask Dr. Stojkova specific questions on this topic. Dr. Andrea Krusi gave a presentation on Qualitative Methods in Health Research Design and answered questions from students following this presentation. Students also introduced themselves and their research project to the group as a way of introduction.

"I enjoyed the workshops as they provide students with tangible skills that will be useful if they choose to pursue research down the road."

-Postgraduate Student Advisor

Workshop 2

The theme of the second workshop was research communication. Here, Michael Unger from SciCATS, gave a presentation on how to present your research to students. We also gave information on the upcoming third workshop which was a student research conference and had a short 30-minute graduate school question and answer session with some of the postgraduate student advisors.

Workshop 3

For the third workshop we held a student research conference. Students built a one-slide poster-like powerpoint and gave a 5-minute presentation on the results of their summer research project to the group with up to 5-minutes of questions from their peers. Students evaluated each other's presentation and the highest scoring presentation won best presentation and received a certificate of award (see Appendix 1 for winning presentation).

Workshop Evaluation

We disseminated evaluation surveys for student feedback to improve future workshops following each workshop. Students were required to attend these three workshops and so besides one or two absent due to illness or previous plans, all students were in attendance. Students rated their experience with the individual workshops and with the workshops overall. We had positive feedback from all three workshops (see Table 4 for individual workshop evaluations). **The majority of students agreed that all three workshops were helpful or information (78%) and the overall satisfaction with the workshops was rated as good to excellent for the majority of students (78%; see Figure 3 for details).**

"I really enjoyed learning about the different forms of quantitative AND qualitative research that can be performed, and both speakers complemented each other well to provide a good introduction to the topic of research methods as a whole."

"Grad Q&A was very helpful to get me thinking more about the future and how the research I'm doing now can help later"

-Student Awardees

Workshops	Percentage of students agreeing that the topic chosen was a good topic for the workshop	Percentage of students agreeing that the overall satisfaction with the workshop was good to excellent
Workshop 1: Research Design	**76%**	**80%**
Workshop 2: Research Communication & Graduate School Q & A	**71%**	**89%**
Workshop 3: Student Research Conference	**89%**	**100%**
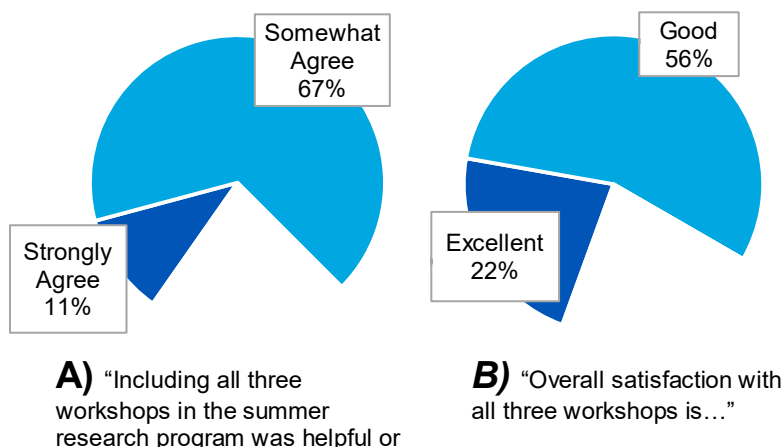
Figure 3. Student responses to prompts shown in figure

A) "Including all three workshops in the summer research program was helpful or

B) "Overall satisfaction with all three workshops is…"

Program Evaluation

Supervisor & Postgraduate Student Advisor Feedback

Once the program was wrapped for the year, we asked supervisors, postgraduate student advisors and undergraduate students to provide us with some feedback on how we did this year and how to improve the program for future years. We received mostly positive feedback with 96% of supervisors reporting that this will generate future research (Figure 4A), 78% believe this has the potential to be included in a publication (Figure 4B), and 79% say this has the potential to positively impact policy, clinical practice, and/or healthcare delivery (Figure 4C). Furthermore, **96% of supervisors said this was a positive experience (Figure 4D) and 83% plan on applying in future years (Figure 4E).**

"This program was crucial in launching a new collaboration between myself and a researcher in the Faculty of Medicine. The results are expected to be used as evidence to support a larger team-grant in Spring 2022, to support a full-scale multi-site research project that will support multiple student researchers."

-Primary FoM Supervisor
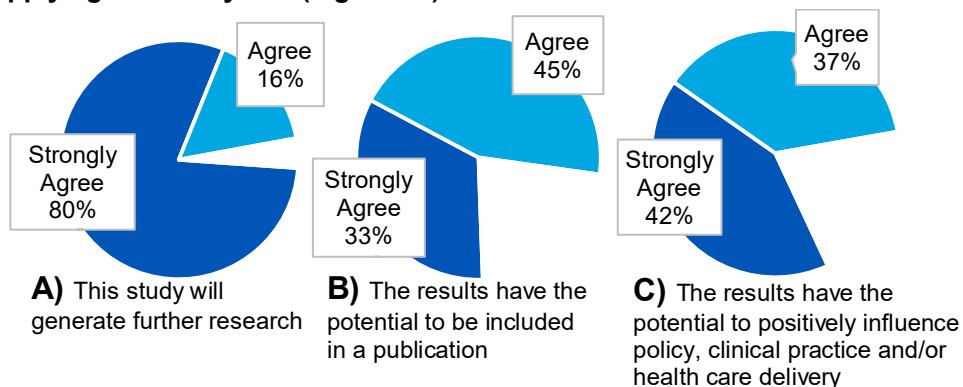
Figure 4. Supervisor and Postgraduate Student Advisor responses to the prompts in figure

A) This study will generate further research

B) The results have the potential to be included in a publication

C) The results have the potential to positively influence policy, clinical practice and/or health care delivery

D) My overall FoM MRPM experience was positive

E) I plan to apply to the FoM MRPM in future
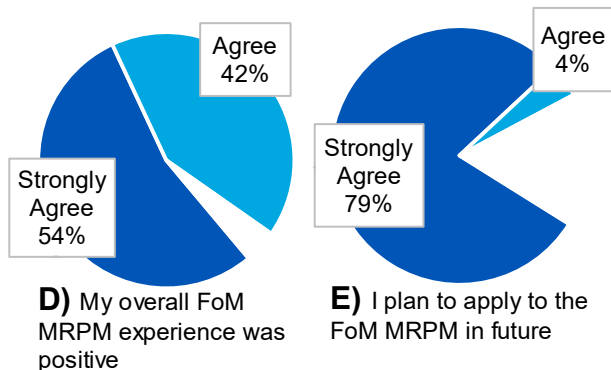
"This is an exceptionally worthwhile program that will create novel lines of research between clinical and experimental faculty."

-Primary FoM Supervisor

Undergraduate Student Feedback

We asked students to provide a project summary to understand the scope of the research undertaken during this year's FoM MRPM pilot program (see Appendix 2 for summaries). We also gathered feedback from student awardees and we again received mostly positive feedback with 100% of students saying that this will generate future research and/or positively influence policy, medical education, clinical practice and/or health care delivery (Figure 5A), 90% of students agreed that they were given the opportunity to interact with and learn from other researchers in addition to their supervisor (Figure 5B), **95% of students rated their overall FoM MRPM experience as positive (Figure 5C), and 95% would recommend the FoM MRPM to other students (Figure 5D)**. Furthermore, this program has facilitated ongoing research opportunities for students with 72% of students agreeing that they will continue working on this project after the FoM MRPM funding ends (Figure 5E) and 100% of students agreed that participating in the FoM MRPM provided insight into potential career goals (Figure 5F).

A) The study will generate future research and/or positively influence policy, medical education, clinical practice and/or health care delivery

B) I was given the opportunity to interact with and learn from other researchers in addition to my supervisor

C) My overall FoM MRPM experience was positive

D) I would recommend the FoM MRPM to other students
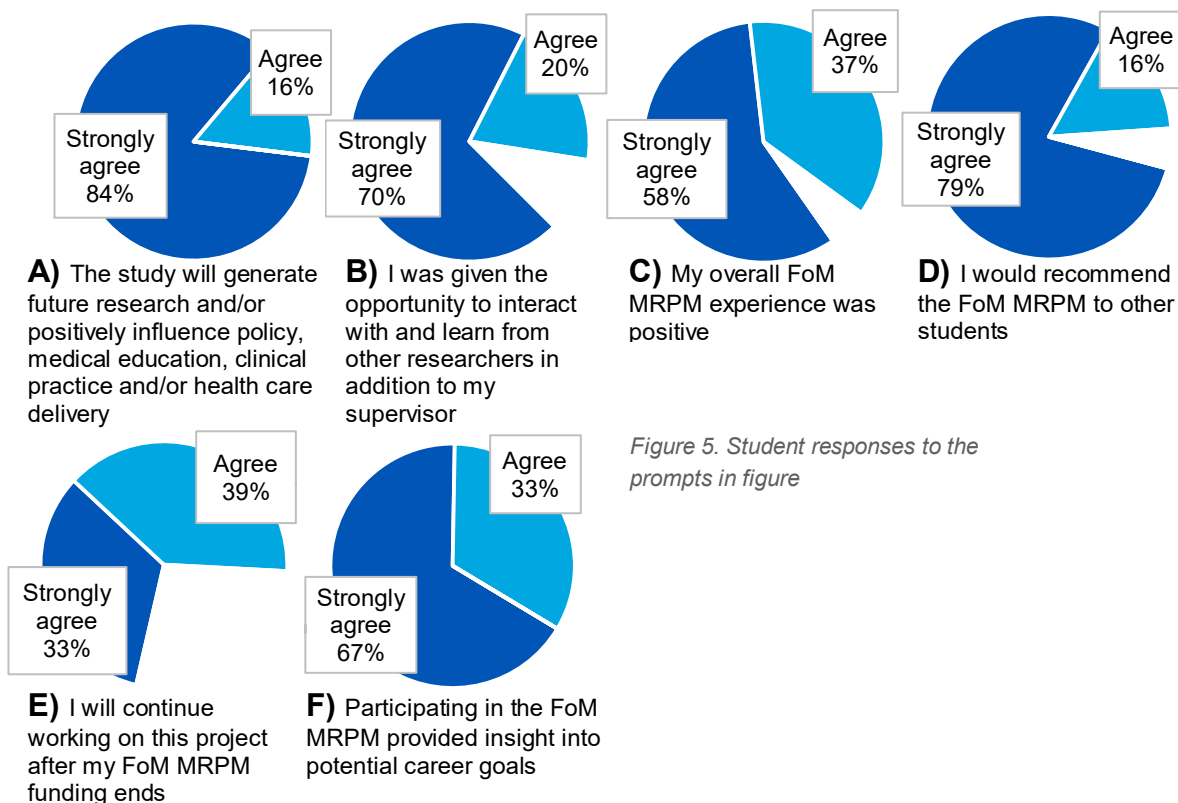
Figure 5. Student responses to the prompts in figure

E) I will continue working on this project after my FoM MRPM funding ends

F) Participating in the FoM MRPM provided insight into potential career goals

"… definitely made an impact on my future career path. I feel a lot more comfortable with concepts outside of my major than I would have had I not participated in the program. I also gained valuable connections to a group of awesome researchers and PIs that I would not have had the chance to meet if I stuck to my own faculty. I also believe the program has given me a very positive outlook on research and makes me more confident in pursuing it."

"… helped me gain a better understanding of what it is like doing research in academia… provided valuable work experience, and in the future, I plan on using this experience to explore more opportunities in multidisciplinary work."

"This experience has enabled me to get better insight on what it is like to conduct basic research. In the future, I will be highly considering graduate studies … I am grateful that I was able to get a look into what research is like early on…."

"…will impact me personally to think out of the box when trying to support my patients."

-Student Awardees

Proposed Program Updates

Changes to the Application Process & Proposed 2022 Timeline

Although we had a successful pilot program in 2021, there are some changes we are proposing based on noted issues with the rollout and supervisor/student feedback.

From the feedback we received it was clear that some supervisors found that there was not enough time for to choose a student partner and that they didn't have enough information on which to base the choice. Therefore, we propose a few changes to the application process to streamline this program in future years:

- Launch Summer 2022 program earlier to give applicants more time (see Table 5 for specific dates).
- Supervisors and students to apply via separate portals. Supervisors to apply for project funding and students to apply directly to the funded project(s) via separate application portals with separate application deadlines. This will also allow supervisors more time to interview students (see Table 5 for specific timeline).
- Students will be asked to upload their CV when applying for a specific project.

We will also be including more information regarding equity, diversity, and inclusion in this project and asking students to self-identify as Indigenous to facilitate Indigenous participation in the program.

Additionally, we had some issues with Postgraduate Student Advisor participation, specifically in the workshops. As this is a non-funded role we are thinking of ways we can get these advisors more involved in the process. Some ideas are to give them a small honorarium, ask students to evaluate their Advisors for future job applications, and/or advertise the role as a formal opportunity to gain supervisory experience necessary for future research careers. All of these ideas will be considered in advance of the Summer 2022 launch.

Task/Item	Previous 2021 Timeline	Proposed 2022 Timeline
Launch/Announce Program	1-Feb-21	15-Nov-21
Close competition period for projects	15-Mar-21	20-Jan-22
Launch/Announce Program	1-Feb-21	15-Nov-21
Send adjudication packages to reviewers for scoring	17-Mar-21	21-Jan-22
Receive adjudicator scores and assign funded projects	28-Mar-21	03-Feb-22
Announce funded projects	31-Mar-21	04-Feb-22
Open student applications	1-Feb-21	11-Feb-22
Close student applications	15-Mar-21	04-Mar-22
Supervisors start interviewing potential students	31-Mar-21	09-Mar-22
Supervisors confirm their student rankings	14-Apr-21	25-Mar-22
Award offers are sent to students	16-Apr-21	29-Mar-22
Formal acceptance deadline	23-Apr-21	05-Apr-22

Table 5. Proposed 2022 timeline details

Appendix 1: Example poster from winning presentation at Student Research Conference during Workshop 3
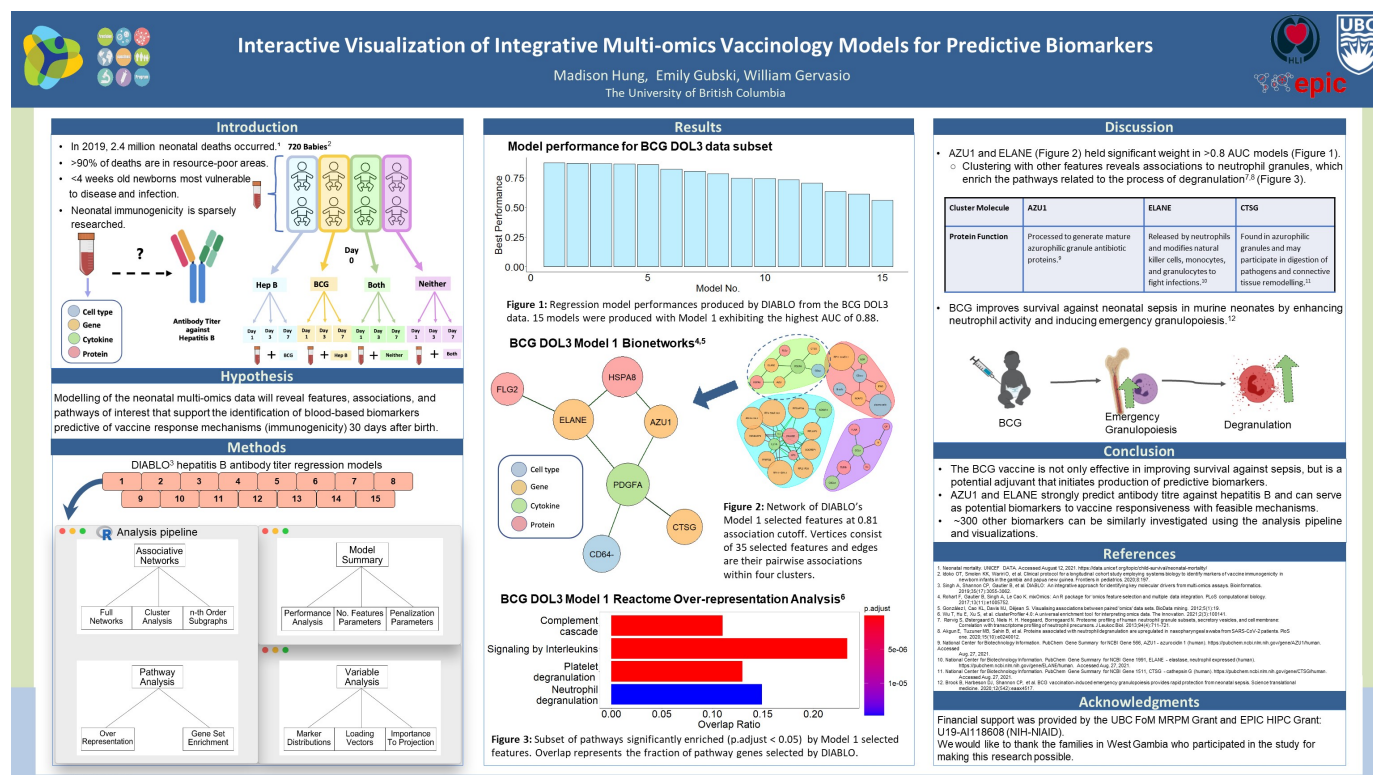
Appendix 2: Project Summaries

Project Title: Measuring balance deficits in chronic inflammatory demyelinating polyneuropathy (CIDP)

What question(s) does your project aim to address?

1. How does CIDP influences balance compared to healthy controls during different phases of IVIg treatment?
2. What is the strength of association between bedside assessments of neurological function and balance and quantitative laboratory measures of balance and sensory functions?

Project Overview

To investigate our research questions, we are aiming to test 15 CIDP patients, as well as their healthy, age-matched controls (individuals who don't have a diagnosis of CIDP and are generally in good neuromusculoskeletal health). With these participants, we engaged in three tests to achieve an overall scope of their individual balance and strength, since the sensory and motor degeneration of CIDP, respectively, manifest in changes in these domains. These three tests included: the SwayStar, maximum voluntary contractions, and a multi-axis tilting platform. The SwayStar is a sensitive gyroscope designed to measure body sway, and consequently infer stability, during simple standing and walking tasks. This measure is intended to establish a baseline of balance that reflects the participant's balance function on a day-to-day basis. To establish a participant-specific baseline for muscle strength and function, maximal voluntary contractions were conducted on a variety of trunk and lower body muscles, with participants contracting their muscles as strongly as possible against resistance applied by the researcher. Finally, the multi-axis tilting platform, on which participants stand upright and are secured by a harness, tilts the participants in four different directions – toes up, toes down, left-side down, right-side down. The task of the participant here is to simply maintain an upright stance before, during, and after the tilting perturbations, which offers a good measure of their dynamic (reactive) balance.

With baseline measures of static (standing) and dynamic (reactive) balance, as well as muscle strength and function, we are looking to run each IVIg-prescribed CIDP patient through the protocol twice, to capture the effects of the IVIg treatment on these functional measures of balance and strength at the beginning of the treatment cycle, versus the end of the cycle.

As one of the two funded undergraduate students on this project, my role involves following the project throughout its entirety, from its conceptualization, through applying for ethics boards' approval, as well as collecting, analyzing, translating, presenting, and disseminating the data. As a current graduate student of the laboratory, this project will inspire follow-up investigations and related projects, which I will likely also spearhead.

Results/Impact

So far, we have collected data from a number of pilot subjects to refine our overall protocol and ensure that all of our methods of measurement are in good working order. Recently, we began collecting our first sets of CIDP patient data and look forward to collecting several more data sets throughout the academic year. Based on past research, we expect that the CIDP patients will have more delayed responses on the multi-axis tilting platform and more instability during the SwayStar stance and gait tasks, in comparison to healthy control subjects. Furthermore, we expect that there will be a temporal association between IVIg treatment and balance performance. Overall, this study intends to improve our understanding of balance control and performance in CIDP patients. As well, we intend to validate clinical outcome measures of balance that can identify the balance and sensory deficits that present in CIDP. Since CIDP is a relatively underdiagnosed and often misdiagnosed disease, the clearer picture of balance deficits may facilitate more effective and accurate clinical diagnosis of the disease. With the potential findings on balance and muscle strength gleaned from this study, we hope to inform and implement non-pharmacological physical or occupational therapy interventions to improve CIDP patients' functional health and overall quality of life. This hope is further fueled by the financial burden that IVIg treatment comes with a high price tag and due to its efficacy, it is often pushed as a front-line treatment that patients will need to take repetitively through maintenance doses in order to suppress the symptoms attributed to their disease. All in all, the findings from this study have the potential to deepen

our overall understanding of balance deficits in CIDP as well as the effects of IVIg in improving these balance deficits. Since CIDP is a disease with many variants, this study may serve as a launching pad for a variety of follow-up studies that dive deeper into different variants or even, other rare neurodegenerative diseases.

Project Title: Biomedical Ophthalmic Imaging of the Retina and Ex Vivo Validation of Cell Degeneration in Mouse Models of Age-related Macular Degeneration (AMD)

What question(s) does your project aim to address?

Given that normal aging is associated with increased drusen deposition, we hypothesize that the increase in drusen and the inflammatory components they contain will correlate with an increase in ADAM10 and ADAM17 as well.

Project Overview

My partner Grace performed Western Blots against ADAMs 10 and 17. The Western Blot is an *in vitro* technique that uses size separation to detect the presence of particular protein in a mixture of cells, in this case were cell contents of o. I performed cell-staining experiments on old and young eyes as well, staining for ADAM10 and ADAM17. Red coloured product was produced using a streptavidin-peroxidase reaction and the eyes were imaged using a brightfield microscope. Preliminary imaging showed that the labeling on old donors was more abundant and more intense than the labelling in the young donors in the choroid, suggesting that there is a higher amount of ADAM10 and ADAM17 in old eyes compared to young eyes.

Results/Impact

ADAM10 and ADAM17 expression was found to be increased in old eyes compared to young eyes, although not significantly. This may be due to the fact that our project is a small-scale study with relatively low power. By increasing the number of donor tissues studied, we could obtain a higher powered conclusion to base following investigations on. Since AMD is an age-associated disease, the implication of using further study to potentially confirm higher ADAM10 and ADAM17 expression in old eyes would mean these ADAMs possibly playing a role in AMD. In the future, if ADAMs are demonstrated to be a major causative agent of AMD, perhaps therapeutic approaches that target ADAM activity has the potential to arrest of slow the progression of AMD and save millions of people each year from severe vision loss. But in the present, future studies would be needed to examine the relationship between ADAMS and drusen formation, in order to hopefully elucidate a mechanism through which these enzymes may contribute to AMD.

Project Title: Cellular and molecular biomarkers to predict vaccine responses in newborns

What question(s) does your project aim to address?
We aimed to use data science, machine learning, and visualization to unveil human molecular and cellular features, known as biomarkers, that predict newborn immune response to vaccination. Furthermore, we sought to identify and explain how BCG vaccine-induced changes in neonatal immune systems consequently improve vaccine response to the hepatitis B virus.

Project Overview
A total of 720 neonates were randomly distributed into different study cohorts. Each study cohort was assigned to specific vaccine schedules in which they undergo their first-round immunization with either the hepatitis B vaccine (HBV), the Bacille Calmette-Guérin (BCG) vaccine, both vaccines, or have both vaccines delayed to their second visit. In both visits, neonates have blood sampled and then receive the required vaccines. These blood samples were processed to draw out datasets consisting of tens of thousands of molecules such as genes, proteins, and cells.

Our MPRM team created a computational analysis pipeline and web application operating on machine learning models of the vaccination datasets. The analysis pipeline extracts multivariate relationships through data science and machine learning techniques to find biological explanations of neonatal immunization. The web application visualizes pipeline results and presents a user-friendly interface for biologists to easily use as a tool to explore important findings and postulate hypotheses.

Results/Impact
Our analysis pipeline and interactive web application provides useful tools for potential biomarker investigation. In preliminary results that only used two datasets, more than 300 biomarkers were identified and constituted potential mechanisms involved in neonatal immunization. These findings provide a grounded basis for further biological investigation to improve vaccine composition or treatments. Overall, knowledge gained from this project will provide valuable insights that can better inform immunization protocols worldwide for millions of newborns.

Project Title: Host signalling as target for TB therpaeutics

What question(s) does your project aim to address?

1. In this study, given the role of GSK3α in TB infection, we ask whether GSK3α can serve as a target for the host-directed therapy of TB. We hypothesize that inhibiting the interaction of GSK3α with Mtb during infection will enhance the macrophage's ability to clear infection, likely through apoptosis, and decrease Mtb survival inside macrophage-like cells.

2. Can the inhibition of a cellular process, phagolysosomal fusion, which helps human cells degrade microorganisms such as Mtb, caused by the protein, PtpA, secreted by Mtb be identified using fluorescence probe technology?

Project Overview

In order to create a scenario where Mtb, or more specifically, Mtb-secreted protein PtpA, cannot interact with and thereby inactivate GSK3α, CRISPR interference was used. CRISPR (Clustered Regulatory Interspaced Short Palindromic Repeats) is a genetic engineering tool used to precisely edit the genetic material of a particular organism in order to cause a gene of interest to lose function or get "knocked-out". In this case, a human macrophage-like cell line, called THP-1 cells, with CRISPR knocked-out (KO) GSK3α gene was generated. Infecting this KO cell line with Mtb essentially stimulates the same effect as a potential host-directed therapy that has prevented the PtpA-GSK3α interaction and will allow us to see if such a therapy will result in less Mtb survival or not.

1. The first part of my contribution to this project was to isolate a KO or non-functioning GSK3α macrophage-like cell line. This first stage occupied the majority of the project's timeline and involved many time intensive KO validation experiments including PCR and Sanger sequencing, RT-qPCR, and western blot analysis. Once a GSK3α KO cell line was confirmed, with the help of my supervisor, I infected the KO cell line as well as the parental cell line (control i.e., functioning GSK3α) with Mtb and analyzed the data to see if the KO cell line had decreased Mtb survival compared to the control.

2. My project focused on developing a fluorescence assay that detects the inhibition of a cellular process, phagolysosomal fusion, in charge of invading and killing microorganisms, such as Mtb. I began my project by purifying PtpA, an Mtb secreted protein, from a batch of *E. coli* cultures. The purified protein,

PtpA, was coupled with latex beads and stained with a fluorescent dye, pHrodo Red. Then, THP-1 human cells were differentiated into macrophages, specialized cells involved in the detection, phagocytosis, and destruction of bacteria and other harmful organisms. The macrophages were then infected with the stained PtpA coupled latex beads and screened on the CellInsight CX5 platform.

Results/Impact

Infection with Mtb resulted in 51% Mtb survival inside macrophages of the GSK3α KO strain compared to 100% Mtb survival in the parental strain at 72 hours post-infection. This result confirms the hypothesis that inhibiting the interaction of GSK3α with Mtb during infection will enhance the macrophage's ability to clear infection and decrease Mtb survival inside macrophage-like cells. With this, we ultimately confirm that GSK3α has a significant effect on the growth of Mtb and identify GSK3α as a target for host-directed therapies against TB. Future studies can further investigate the role of GSK3α in TB infection by measuring apoptosis in the KO cells compared to the parental cells. Such a study would confirm that the decreased Mtb survival in the KO strain is in fact due to the inhibition of anti-apoptotic activity.

This study demonstrates that GSK3α inhibitors are promising compounds to be evaluated as HDTs for TB and provides evidence that targeting host kinases, such as GSK3α, is an effective approach for the development of HDTs. Given that TB contributes to nearly 2 million deaths each year and remains one of the top 10 causes of death worldwide, the results of this project can guide the development of novel therapies and make the goal of eliminating TB more attainable.

Project Title: Woodsmoke exposure-on-a-chip

What question(s) does your project aim to address?
Cells exposed to woodsmoke will exhibit higher oxidative stress, release more inflammatory cytokines, and experience greater cytotoxicity.

Project Overview
The project Woodsmoke Exposure on-a-Chip consists of 3 main components: cell culture, production of the working chip, and woodsmoke exposure. The chips are the microfluidic device that mimics complex structures and functions of living human organs. It is size approximates that of USB and is made of polydimethylsiloxane (PDMS) with a polyester (PET) membrane insert. Organ-on chips can contain differentiated mucociliary bronchiolar epithelium and an underlying microvascular endothelium and experiences fluid flow. It enables research on a wide range of human diseases and possible treatments. The lung epithelial cells are cultured in the flask for about 12-14 days until confluent. The cells are seeded into the chip and cultured until differentiation. The cell containing chips connect to a specially designed airflow system that provides aerosol woodsmoke to the cell within the chip. With the successful 3 components, the differentiated lung epithelial cells can be observed and how they react with the woodsmoke exposure.

Results/Impact
With the limitation of the time, our minimal conclusion is that statistically significant differences were not found in both cytotoxicity and inflammatory mediator upregulation. Through this study we had some limitations such as irregular effluent collection due to chip leakage or contamination Because of this, the cells were not able to be fully grown and differentiated. As in future directions, we suggest using ZO-1 tight junction staining to visualize barrier integrity in epithelial layer and optimize chips for 30-day differentiation which will enable us to culture more range of cells. Furthermore, with more revised design of chip can lead the research to culture more various type of cells to experiment with.

Project Title: Establishing a data processing pipeline using artificial intelligence to capture human kinematic data: DeepLabCut as a markerless motion capture system

What question(s) does your project aim to address?

What is the feasibility of using artificial intelligence-informed approaches, including DeepLabCut a markerless motion capture system, for analyzing complex human kinematic data?

Project Overview

The purpose of this research is to investigate the feasibility of a markerless motion capture system: DeepLabCut, for use in studies of human motor learning. Deliverables of the proposed project include:

1. Development of a data processing pipeline to analyze kinematic variables from a neural network created by DeepLabCut
2. Assess DeepLabCut's ability to discriminate and generalize amongst a variety of movements in a healthy population, relative to other available video-based motion capture systems, such as DartFish or Kinove.

In this project we created a project pipeline for future research studies to use DeepLabCut to analyse the movement data collected. This involved installing DeepLabcut on personal and lab computers, optimising the workflow to train the AI network initially, and recruiting the use of Sockeye, UBC's supercomputer, to help with the speed of analysis. We investigated the number of frames that had to be labeled by a human to train the AI network, and determined best practices for using sockeye to analyse DeepLabCut. We tested the efficacy of DeepLabCut by training the AI network on one participant's movement video and testing the network on new, unseen participants videos. We also carefully documented our process for future researchers wanting to use DeepLabCut.

We collaborated and met regularly (on a weekly basis) with project supervisors, the postgraduate student advisor, and graduate student trainees on the research team. We began our process by reading previous research and evidence that has been used to develop the rationale for this study, ensuring that we were oriented to the field. We then created and tuned a neural network for analysing Dart throws, and refined the processing pipeline to remove technical bugs.

Results/Impact

We determined the feasibility of the machine learning software DeepLabCut and found that it was able to accurately analyse movement patterns and dramatically decreased the amount of human intervention to extract kinematic data from human movements. Furthermore, it decreased the amount of total time required to analyse a data set and output results in a way that was easily exportable to other formats. The software and process was also deemed to be user-friendly, and thus a feasible alternative to existing motion capture systems.

Next steps of this project involve analysing multiple movement patterns and using a sister software called B-soid to aid with the behavioural segmentation of data. Furthermore, we aim to ultimately test the efficacy of this software with clinical populations and check feasibility using videos captured in a low quality camera. This is to determine the use of DeepLabCut when analysing video data captured on a phone by a stroke patient in their own home and ultimately increase the feasibility of Telehealth based movement assessments for clinical populations.

Overall, the usefulness of DeepLabCut is in its potential to assess physical movement conveniently. DeepLabCut has removed the need for conventional marker-based motion capture systems. So, in the future, it could be used to remotely conduct physical assessments from the comfort of a patient's home with high quality and accuracy of the data obtained. This will benefit the large population of patients with movement disorders including neurological, psychiatric, and rehab patients.

Project Title: Three-dimensional, microscale in vitro model for studying axon growth

What question(s) does your project aim to address?

Can neurites regenerate within the artificial spinal cord model? Can magnetic microrods be aligned within the model? Is this model ideal for measuring neurite regeneration?

Project Overview

A chip designed to represent a spinal cord was developed and fabricated from Polydimethylsiloxane (silicone), commonly used for microscale models. Primary neurons were harvested from rat pups and incorporated into the chip within a gel to allow them to grow in a 3D environment within the chip. The neurons within the chip were allowed to grow and neurites to extend. The "spinal cords" then had a portion removed to represent an acute spinal cord injury. The neurons were allowed to grow for 7 more days and then they were fixed, stained, and imaged to examine neurite regeneration within the chip. Modifications were made over time to the chip design to improve ease of use and replicability for experiments.

A large focus of the project (and my primary responsibility) was on inclusion of magnetically alignable microrods within the model. A protocol for designing magnetic microrods was developed in-house using polycaprolactone (a well-known biocompatible polymer) and superparamagnetic iron oxide nanoparticles (responsible for the magnetic activity of the rods), and the protocol was optimized over the summer. Out-of-house magnetic microrods were obtained from a partner lab using them within mice and were used to confirm alignment within the *in-vitro* model in different directions, at different magnetic field strengths, and over time. Microrods were suspended in a gel and allowed to fill the injury location within the chip, before being aligned within a magnetic field and the gel crosslinked to "lock" the rods into place. Directionality of the rods after alignment was quantified via a software-based orientation analysis to confirm that alignment was achieved.

Results/Impact

Neurites were shown to grow within the developed *in-vitro* model. The primary neurons used in experiments exhibited outgrowth within the chip. The microscale *in-vitro* model is therefore suitable for neurite outgrowth studies using primary spinal cord neurons. This result is key in establishing the model for future studies on regeneration of the spinal cord *in-vitro*. This will allow research on therapeutics targeting regeneration of neurites potentially higher throughput then current efforts using animal models.

Magnetic microrods were demonstrated to be aligned and maintain alignment within the *in-vitro* model. This preliminary data is promising and verifies the value of this microscale *in-vitro* model for future experiments on alignable magnetic microrods as treatment options for spinal cord injury. Data collection on how the injectable, alignable scaffold influences neurite outgrowth can now begin, which could allow for the discovery of a promising new facet of treatment for spinal cord injury and opens the way for investigations into the mechanisms behind why neurites seem to grow in an organized fashion within a unidirectionally patterned environment.

Project Title: Non-invasive neuromodulation for treatment of autonomic dysfunctions after spinal cord injury

What question(s) does your project aim to address?

In the current project, we aimed to evaluate whether the TCS will ameliorate both cardiovascular and bowel dysfunction in a well-established contusion rodent model. One of our targets included standardization of a procedure to measure bowel dysfunction in our rodents. We hypothesized that non-invasive stimulation of the spinal cord below the level of injury will modulate autonomic function following SCI.

Project Overview

We used a well-established and clinically relevant rodent model (rat) where we performed a contusion spinal cord injury at the third thoracic segment (T3). After the injury, animals remained undisturbed for a total of four weeks and then implanted with a wireless blood pressure transducer. Bowel distention, a clinically observed AD trigger, was instigated using a balloon-tipped catheter to reliably induce AD. Simultaneously, a group of animals were separated for the anorectal manometry procedure, which was used to characterize the bowel dysfunction by measuring the rectal pressure. A balloon-tipped catheter was inserted inside the rats' rectum at multiple levels and the rectal pressure was measured before, upon and after the inflation of the balloon.

1. As part of my role, I interacted with the experimental animals, which included surgical preparation, daily animal care, experimental AD assessments, and anorectal manometry measurements. Following data collection, I was responsible for extracting the data from the collection software, and comparing blood pressure and heart rate values before, during and after the experimental AD episode. An AD episode is defined as a set increase in blood pressure; therefore, part of my role was to calculate whether bowel distention led to an AD episode based on the definition. In addition to this project, another project overlapped with the award timeframe, where I oversaw an entire project examining the neuroprotective roles of various pharmaceutical agents for spinal cord injury and cardiovascular dysfunction. This included planning logistics, performing essential procedures, and coordinating resources.

2. As part of my role, I interacted with the experimental animals, which included animal handling, subcutaneous injections, surgical preparation, and daily animal care. In addition to this project, some animal procedures also overlapped with another project occurring in the award time frame, where we observed the effects of various neuroprotective drugs for which quantification is still in progress. As such, I was able to perform histological analysis on the spinal cord cross section samples. Coming from a clinical background, this project gave me the opportunity to work in a pre-clinical setting and familiarize myself with the protocols involved in animal studies.

3. A literature search of the databases for publications from the inception dates of the databases up to May 21, 2021, was conducted to identify those that looked at spinal cord stimulation on humans and reported heart rate, blood pressure, and heart rate variability results. As most publications were case studies, these were included. Ultimately, 1909 publications were identified and filtered down to 47 after the careful removal of irrelevant or duplicate results. From the final selected studies, stimulation methods, settings, and outcomes were extracted, and qualitative results were compiled.

Results/Impact

Regarding the cardiovascular objective, similar to the previous pilot study with the transection model, the TCS led to interruption and prevention of AD episodes. Although the determination of efficacy of long term TCS on bowel dysfunction is still in progress, our current study was able to establish a clinically relevant model of bowel dysfunction following SCI in rodents.

The results obtained from this project could be implemented in the clinical model for further studies. In addition, the results of the study could guide the development of management strategies addressing understudied priorities of SCI patients and ultimately improving patient quality of life. We further believe that the findings of this study should be further investigated to understand the cellular mechanisms of TCS and its possible efficacy in recovery of other crucial functions such as in the genitourinary systems.

Project Title: Development of universal/stealth red blood cells by novel cell surface engineering methods

What question(s) does your project aim to address?

We hypothesize that polymerization of a polysialic acid layer on the red blood cell surface would camouflage minor antigens like the Rh D antigen, thereby preventing immune recognition of the Rh D antigen. This would reduce the risk of severe immunological reactions in a blood transfusion recipient as well as create a greater inventory of compatible RBCs available for blood transfusions.

Project Overview

This project employs an enzymatic approach to polymerize polysialic acids (PSA) on the RBC surface in order to create a pseudo-layer of PSA that mimics the glycocalyx. The glycocalyx is a sugar-based layer that covers the RBC surface and consists of sugars known as sialic acids. Our approach involves polymerization of a PSA layer using these sialic acids already present in the glycocalyx. In this method, PSA is synthesized on the RBC surface by adding a polysialyltransferase enzyme and its substrate. My role in this project was primarily focused on the characterization of RBCs modified using this enzyme as well as subsequent investigation for any immune response generated towards the modified RBCs.

First, we focused on developing a protocol for using a polysialyltransferase enzyme to modify the RBC surface. The protocol was optimized to find the optimal enzyme as well as substrate concentration. Further optimization entailed finding the best temperature and time required for incubating RBCs treated with the enzyme. After enzyme treatment, the efficiency of the polysialyltransferase enzyme in creating an immunocamouflage was evaluated using a clinically validated assay which employs antibodies that are specific for the Rh D antigen. This method is used to observe any agglutination against the Rh D antigen where no agglutination indicates successful immunocamouflage effect. Next, the polysialylation of the RBC surface was confirmed using flow cytometry. This was done in order to show that the enzyme was successfully polymerizing PSA on the RBC.

The second part of this project focuses on testing for any immune response towards the modified RBCs. This involves conducting serology tests on the modified RBCs which refers to using human serum for identifying whether antibodies against the Rh D antigen are present on the RBC. These antibodies are primarily of the IgG type and by using anti-IgG antibodies, we can clinically determine whether an immune reaction occurs. Currently, we are also using another clinically validated assay using different immune cell lines to determine whether the modified RBCs are detected as foreign by innate immune cells.

Results/Impact

The results from this project so far show that our enzyme is successful in adding polysialic acids to the RBC surface. By treating RBCs with our polysialyltransferase enzyme under optimized conditions, we were also able to show successful immunocamouflage effect using a clinical assay. Under optimized conditions, we have also shown that the anti-IgG antibodies in serology studies conducted did not agglutinate with the modified RBCs. Further investigation is still being conducted using human immune cell lines.

Shortage of blood supply continues to be a major issue in transfusion medicine due to lack of availability of rare blood groups. Mismatch of Rh D antigens during blood transfusion also creates risk of acute transfusion reactions in patients. We hope to address these challenges by enzymatically building polysialic acids on the RBC, thereby successfully concealing the Rh D antigen from immune system detection. We hope that this would help make blood transfusions safer and more readily available for patients.

Project Title: A biomaterials-based platform coupled with drug delivery to induce nerve repair after spinal cord injury

What question(s) does your project aim to address?

Can biomaterials-based, porous microchannels be sequentially injected *in-vitro* and magnetically aligned while retaining their hollow shape?

Project Overview

A minimally invasive alternative is required to guide growing axons across the injury site, and thus singular injectable microchannels have been developed. Multiple microchannels will be sequentially injected into the injury site of a spinal cord and assembled *in-vivo*, thus providing the physical guidance for induced axonal growth. The developed microchannels are composed of a biomaterials-based polymer, sodium chloride particles, and magnetic nanoparticles. The sodium chloride particles' role is to form pores in the polymer structure, which is achieved by removing the sodium chloride from the formed microchannel through dissolution. In the process, holes, or pores, remain where the particles once were. These pores are a crucial addition as they allow for essential nutrients to reach the axons that are growing through the injected microchannels. The magnetic nanoparticles are added to allow for magnetic alignment of the channels, ensuring their correct orientation and therefore the correct guidance of the axons. The microchannels are aligned by responding to an externally applied magnetic field.

To fabricate the channels, a thin wire is drip-coated into a solution containing the polymer, sodium chloride, and magnetic nanoparticles. The microchannels are allowed to completely dry then removed from the wire, forming the hollow channels, which are then placed in water to allow the sodium chloride to dissolve out of the structure. Finally, the microchannels are placed into a syringe, injected *in-vitro*, and aligned magnetically.

My role in this project was to optimize the composition and fabrication of the biomaterials-based polymer solution such that the hollow microchannels remain open after being forced shut, as in the case when being injected via a thin needle tip. In addition, I conducted testing to inject and magnetically align the microchannels in-vitro by applying an external magnetic field to the channels.

Results/Impact

The results showed that the composition of the injected microchannels allowed for them to remain open and hollow. The microchannels were successfully magnetically aligned *in-vitro*, indicating the potential for the correct assembly and alignment along the spinal cord in the injury site. In addition, microscopy revealed evenly distributed, interconnected pores within the structure of the microchannels.

These microchannels can provide an improved alternative to invasive multi-channeled implants, thus providing a lower risk and less damaging option for the treatment of spinal cord injuries.