THE UNIVERSITY OF BRITISH COLUMBIA
Faculty of Pharmaceutical Sciences

UNDERGRADUATE SUMMER STUDENT RESEARCH PROGRAM (SSRP)
2023 PROJECT LIST

Content updated: January 19, 2023

Projects are posted in the order in which they are received. **Please keep checking the website as this list may be added to until the application deadline**

Projects:

Summer Student Research Program Project Description

Project #: SSRP23-Min/Leung
Supervisors: Jason Min; Larry Leung
Project Title: Improving Community Pharmacy Access in Remote First Nations Communities

This project is only eligible for the Indigenous Undergraduate-SSRP (IU-SSRP) funding stream (i.e. only eligible Indigenous undergraduate students are invited to apply).

Hypothesis or Research Question being addressed:

- How can community pharmacy services and access be improved?
- What does the community want to see in future community pharmacy services?
- How can pharmacy be better integrated into new health center services?

Project Description:

Five neighbouring remote First Nations Communities in British Columbia are partnering with the UPROOT Team at UBC in the development of innovative health centre services to improve equitable access to care for community members. Current medication and pharmacy service access is limited by poor road conditions and a lack of delivery services from the nearest pharmacy, resulting in delayed starts to crucial medications and reduced medication adherence. The health centre honours the self-determination and leadership of each individual Nation and offers unique opportunities to build new models of care suited to their specific needs. Currently, there are plans for improved interprofessional collaboration and better integration of existing health services. However, pharmacy services and access are not part of any immediate plans.

The primary goal of this project is to improve pharmacy service access for the five communities by taking a community-based approach to better understanding these interprofessional opportunities for integration in the future.

In this SSRP position, the student will participate in the following activities:

- Conduct a thorough environmental scan of existing pharmacy services in the neighbouring communities
- Collect and analyze quantitative and qualitative survey data
- Utilize a community-based participatory action research methodology for community partner engagement
- Interview Indigenous community partners and stakeholders
- Create a summary report of key findings

Proposed Research Approach

We will apply a two-eyed seeing approach to integrate Western evidence/knowledge with local, traditional protocols and preferences as it relates to this community-based research project. We commit to continuing our flexible approach, prioritizing the autonomy of the communities, emphasizing reciprocity, and using an asset-based mindset to:

1) Take time to deepen existing relationships through ethical engagement, following Nation-specific protocols, and offering in-person and virtual modalities
2) Take time to listen and share ideas throughout

3) Provide a feedback and accountability process for community members and partners to share openly and safely any opinions throughout. This will include regular check-ins with partners, anonymous surveys, and in-community townhalls.

Expected Project Outcomes

1) One summary of community engagement activities and findings
2) One summary of western literature on the topic, a scoping review of other Indigenous-led primary care and pharmacist service initiatives, inclusion of new Ministry of Health scope of practice and funding models as a way to support sustainability
3) One final summary report with all of the findings and recommendations for implementation at their health centre
4) Presentation of the final summary report back to the partner communities at their discretion and preference for method and forum.

Qualifications:

- An Indigenous undergraduate student enrolled in an undergraduate program at the University of British Columbia
- Interest in Indigenous health, cultural safety, and community engagement
- Proficient knowledge of basic office computer software (e.g. Microsoft Word, Excel)
- Ability to show initiative, good judgement, time management skills, and professionalism
- Be able to work independently, and meet deadlines as agreed upon
- Excellent communication skills, both written and verbal

Summer Student Research Program Project Description

Project #: SSRP23-Wong-01
Supervisors: Judy Wong
Project Title: G-quadruplex and Telomere Recombination

Hypothesis or Research Question being addressed:
G-quadruplexes are hallmarks of Alternative Lengthening of Telomere cancers which could be exploited for therapeutic development and clinical management of these cancer types.

Project Description:
Telomeres cap the ends of linear chromosomes and serve as a mitotic clock to limit the number of divisions in a cell lineage. To overcome this proliferative barrier, more than 85% of human tumors reactivate the telomere-repair enzyme telomerase (TERT). The remaining 15% are TERT-negative, utilizing the alternate-lengthening-of-telomeres (ALT) mechanism, a non-reciprocal homologous recombination-based telomere-repair process. ALT tumors do not express TERT; they show higher expression of recombination factors, and frequent genetic changes indicate hyperactive homology-directed recombination. ALT tumors were found to be frequently associated with mutations in the alpha thalassemia mental retardation syndrome X-linked protein (ATRX), an SWI/SNF chromatin remodeler. Loss of functional ATRX correlates with chromatin structural changes essential for telomeric recombination.

Persistent telomeric DNA damage signals in ALT tumors are essential for initiating the illegitimate recombination mechanism for telomere elongation. Our recently published data suggested that G-quadruplexes (G4), a noncanonical nucleic acid structure formed in G-rich genomic regions, provide this DNA damage initiation signal. Nuclear G4 is found significantly enriched in ATRX-/- primary glioma samples and colocalized with DNA-RNA hybrid structure (R-loop) at ALT telomeres. We further demonstrated that telomeric G4 and R-loop are spatially linked and positively influence each other's stability. Pharmacological stabilization of both G4 and R-loop can cooperatively enhance ALT activity (hyper-ALT) at sub-lethal doses, and that higher doses of cotreatment led to synergistic cytotoxicity. Together, these observations support the formation of unique genomic structures comprising co-existing G4s and R-loops on opposing strands, which play essential roles in stimulating ALT telomeric recombination.

In this project, we will test the utility of G4 as a diagnostic marker for the ALT telomere maintenance mechanism with clinical samples collected from relevant cancer types. We also intend to test the therapeutic utilities of G4-stabilizing ligands and inhibitors of cellular helicases responsible for the resolution of G4s. ALT is found in the most clinically challenging cancer types, such as pediatric and adult brain cancers, soft tissue sarcoma and osteosarcoma, with limited therapeutic options. The lack of identified ALT tumor-specific targets has restricted the development of clinical interventions. Our data will improve the current understanding of the molecular features of ALT tumors and provide strategies for targeted therapeutic interventions. Notably, newer G4 ligands are currently being tested in clinical trials against BRCA-negative breast cancers, with encouraging results. Successful implementation of our plans will have immediate translational potential by extending clinical testing of these novel agents to ALT-tumor subtypes.

Qualifications:
The successful candidate should be currently enrolled in degree programs, including pharmacy, pharmacology, biochemistry, molecular biology, or a related discipline. Preference will be given to those with experience in molecular biology, genetics or genomics research. Must have all recommended

vaccinations for working with human cells and clinical specimens and be comfortable working with human materials. Excellent interpersonal and communication skills and the ability to work in a collaborative team or semi-independently as needed.

Summer Student Research Program Project Description

Project #: SSRP23-Wong-02
Supervisors: Judy Wong
Project Title: Non-canonical DNA Repair Activities of Human Telomerase Reverse Transcriptase

Hypothesis or Research Question being addressed:
Telomerase promotes cell survival following cytotoxic and metabolic stress and abets growth and proliferation through participation in multiple structural complexes.

Project Description:

Chromosome ends are capped by protective DNA-protein structures known as telomeres. Telomeres become shorter with each cell division, causing a gradual erosion of the protective cap. When telomeres become critically short, cells stop dividing. In some specialized cells that require extended proliferation lifespans, such as stem cells and germ-line cells, telomeres are intermittently repaired by the enzyme telomerase. This repair process extends the proliferative capacity of these cell types. Accordingly, genetic changes affecting telomerase activity are associated with a spectrum of inherited diseases with cellular renewal defects, collectively known as telomere biology diseases. On the other hand, tumor cells exploit this endogenous repair system by increasing the activity of telomerase to escape the cellular limit on their growth. Notably, over 85% of human cancers are found to have an overabundance of telomerase activity through the upregulation of the telomerase reverse transcriptase (TERT) subunit.

New evidence suggests that TERT expression promotes cell survival under stressful growth conditions through multiple mechanisms. One of these mechanisms involves increasing the cellular tolerance against DNA damage to the nuclear and mitochondrial genomes. These survival advantages provided by TERT are mediated through cellular functions unrelated to telomere repair. However, the precise biological pathway and TERT's structural form responsible for these activities remained largely unknown. A complete understanding of the spectrum of TERT's non-canonical activities and how these activities are regulated in response to changes in the growth environment is essential to comprehend the enzyme's roles in health and diseases.

We will perform BioID labelling and LC-MS-MS analysis of TERT-interacting partners. Following the identification of novel TERT interacting partners, we will validate the presence of TERT-containing complexes using telomerase-positive human cells. The biological functions of selected non-canonical TERT complexes will be evaluate with genetic and/or pharmacological means. Our comprehensive study aims to purify and identify different TERT complexes responsible for their canonical and non-canonical functions. Our functional and biochemical characterization of the different TERT structural forms and their membership in unique biological complexes will further understand the plethora of telomerase activities in health and diseases.

Qualifications:
The successful candidate should be currently enrolled in degree programs, including pharmacy, pharmacology, biochemistry, molecular biology, or a related discipline. Preference will be given to those with experience in molecular biology, genetics or genomics research. Must have all recommended vaccinations for working with human cells and clinical specimens and be comfortable working with human materials. Excellent interpersonal and communication skills and the ability to work in a collaborative team or semi-independently as needed.

Summer Student Research Program Project Description

Project #: SSRP23-Finbloom
Supervisors: Joel Finbloom
Project Title: Nanoparticle Drug Delivery to Treat Bacterial Infections

Hypothesis or Research Question being addressed:

Antibiotic resistance is a global health crisis, with antibiotic resistant bacterial infections posing significant challenges in clinics throughout the world. This project aims to develop a nanomedicine approach to better deliver antibiotics to bacterial infections and overcome antibiotic resistance mechanisms. The central hypothesis of this project is that polymeric nanoparticles loaded with antibiotics will enhance antibiotic penetration and distribution into the bacterial infection space, increasing anti-bacterial properties when compared to antibiotics treatment alone.

Project Background and Significance:

Antibiotic resistance is a major global crisis, recognized by the World Health Organization as a dire threat to human health. One of the major causes of resistance is the growth of bacterial biofilms, where bacteria encase themselves within a dense network of biomolecules such as polysaccharides, DNA, and proteins. These biofilms prevent drugs such as antibiotics from reaching their bacterial targets, rendering them ineffective. Furthermore, bacterial biofilms lead to complex chemical environments that vary in pH and oxygen levels, altering bacterial behavior and further reducing antibiotic effectiveness. These bacterial biofilms occur in approximately 80% of human infections, and can be over 1000-times resistant to antibiotics when compared to free-floating bacteria.

Project Rationale and Hypothesis:

Nano-scale materials can offer advantages in the treatment of bacterial infections, as these “nanoparticles” are on the same size-scale of the bacterial biofilm components and can be loaded with antibiotics to improve drug delivery. Students working on this project will create nanoparticles loaded with antibiotics and will engineer the surface chemistry of the nanoparticles to better direct their navigation within bacterial biofilms. By directing nanoparticle navigation to the desired regions of the bacterial biofilms, we hypothesize that nanoparticle drug delivery will improve antibiotic activity when compared to standard antibiotic treatment approaches.

Project Approach:

Students will fabricate nanoparticles made of biodegradable polymers and optimize fabrication techniques to improve drug loading levels. Antibiotic drugs such as tobramycin will be used throughout the studies. In addition to optimizing drug loading, students will also design nanoparticles with different surface components. These surface structures will alter nanoparticle properties such as charge (positive, negative, or neutral) and hydrophobicity/hydrophilicity, which will guide nanoparticle interactions with bacterial biofilms. Nanoparticles will be characterized using materials science and chemistry techniques such as dynamic light scattering, electron microscopy and zeta potential surface charge measurements. Drug release will be monitored using benchtop techniques such as absorbance and fluorescence measurements. Lastly, students will test nanoparticles for antibiotic activity and compare the bacterial growth rates of nanoparticle-treated bacteria against those treated with antibiotics alone and no-treatment control groups.

Project and Learning Outcomes:

By the end of the project, students will have fabricated polymeric nanoparticles, loaded nanoparticles with antibiotics, and evaluated nanoparticle drug delivery in bacterial cultures. Students will receive direct supervision under Dr. Finbloom and will learn all relevant techniques for this project, ranging from nanoparticle fabrication to bacterial techniques. Additionally, students will gain experience in project development, experimental planning, and science writing and communication.

Qualifications:

Research in the Finbloom lab is highly interdisciplinary and students will receive training in a variety of skills including nanomaterial fabrication and characterization, biochemical techniques, organic chemistry, and microbial culture and imaging. Dr. Finbloom emphasizes a growth mindset approach to learning and works closely with students to develop and execute research projects and communicate their scientific research in both written and oral forms.

Relevant coursework and/or laboratory experience in pharmaceutical sciences, microbiology, organic chemistry, and/or bioengineering is preferred. The project would be well-suited for a student interested in pursuing graduate-level research in Pharmaceutical Sciences, Chemical Biology, or Bioengineering.

Summer Student Research Program Project Description

Project #: SSRP23-Ross
Supervisors: Colin Ross
Project Title: Lipid nanoparticles for gene therapy and genome editing

Hypothesis or Research Question being addressed:
Our hypothesis is that we can improve the efficacy and safety of genome editing by using lipid nanoparticles (LNPs) to deliver gene editing components to cell lines. Our specific research question for this project will be to investigate novel lipid formulations and novel genome editors for their efficacy and safety of genome editing. Our lab is collaborating with the Cullis lab for access to novel lipid nanoparticle formulations that will be tested. In addition, we have developed several novel base editor formulations to examine both their efficacy and safety.

Outline of research project:
This project will investigate using lipid nanoparticles (LNPs) as a method to deliver gene editing components to cell lines with the goal of improving both the LNP delivery system and gene editing efficiency. Gene editing has the potential to correct thousands of genetic diseases which currently have no treatment options. This project will primarily use base editors – a technology which corrects single nucleotides at a specific site in the genome which is designated by a guide RNA. To effectively correct a cell, both the base editor and the guide RNA must be able to get inside the cell. The project will use different LNPs to deliver mRNA which encodes for a base editor and guide RNA. LNPs have an advantage over current systems as they are less toxic to cells and can be more easily translated to animal models. The student will learn how to conduct mammalian cell culture and will administer LNPs to different cell lines. They will be responsible for the data collection within this project with the ultimate goal of identifying a top LNP for transfection of cell lines and an optimized protocol to use within this project. The summer student will be involved in all steps of this project – from learning about experimental design to analysis of results.

Student responsibilities:
The student will be responsible for several tasks, for which they will receive detailed hands-on training beforehand. A typical week will consist of (1) maintenance and plating of cell culture colonies, (2) transfecting cells with LNPs, (3) preparing cells for flow cytometry, and (4) conducting and analyzing flow cytometry experiments. The student will learn proper aseptic technique and protocols for the care and maintenance of HEK293T cells. Flow cytometry is a powerful tool to analyze editing efficiency – the student will learn how to remove cells from a plate and prepare them for analysis. The student will be taught how to run a flow cytometer and analyze the results. These skills are highly transferrable to other labs and industry, providing the student with valuable knowledge. There are opportunities for the student to learn a wider array of techniques if they are interested as well including PCR, DNA sequencing and bacterial cloning.

The student will work closely with a PhD student, Tessa Morin, with whom the student will be interacting with daily. The student will meet at least two times a week with Dr. Ross including a 1 hour lab bench-side discussion on weekly progress. The student will attend weekly lab meetings as well where they will be able to present their results and receive support from a wider team. At the end of the summer the student will present their poster at the SSRP poster competition.

Skills gained:
- Mammalian cell culture & transfection protocols. Biosafety and chemical safety

- Flow cytometry, PCR, DNA extraction & DNA sequencing, and gel electrophoresis
- Cloning, bacterial culture, gene therapy, gene editing

Qualifications: The student will be taught all relevant techniques but previous knowledge in genetics, basic laboratory techniques and biochemistry is an asset.

- 2nd or 3rd year in a BPSc (or similar) with an interest in gene editing and gene therapy.