College of Pharmacy Undergraduate Summer Research Projects

PROJECT #1

PI Name (Last, First):	**Stobart, Jillian**
PI Email:	**Jillian.stobart@umanitoba.ca**
Please advertise to students on my behalf: (yes/no)	**Yes**
I will approach a student myself: (yes/no)	**Yes**

Project Title: Brain pericyte calcium signaling and blood flow control in a mouse model of Alzheimer's Disease

Short Description of Research:

Pericytes are cells found on brain capillaries. Exciting new evidence suggests that pericytes may regulate the blood-brain-barrier and dilate capillaries to increase blood flow where needed. Both of these roles are essential for brain health and pericytes may become dysfunctional or die during Alzheimer's Disease (AD). Our research focuses on calcium signalling in pericytes, which is likely important for regulating blood flow. We want to know: how do calcium signals in pericytes and brain blood flow change over the disease progression in a mouse model of AD? Does this correspond with changes in memory? Why do these changes occur? These questions are fundamental for understanding pericyte pathophysiology and their role in AD. This work may also lead to future development of pericyte-specific drugs for therapeutic use. Students who join our energetic team will have the opportunity to work directly with mice, including mouse handling, training, injections, and memory testing. Students will also learn two-photon microscopy, the latest, state-of-the art microscopy technique in neuroscience. They will use this microscope to record movies of never-before-seen calcium signals in pericytes in the brains of live mice in real-time. Students will also gain valuable computer skills by learning to analyze these calcium movies through programs such as MATLAB and R. Additionally, students will also develop communication and problem-solving skills by participating in regular lab meetings in a group setting.

PROJECT #2

PI Name (Last, First):	**Maruf, Abdullah Al**
PI Email:	**abdullah.maruf@umanitoba.ca**
Please advertise to students on my behalf: (yes/no)	**Yes**
I will approach a student myself: (yes/no)	**No**

Project Title: Pharmacogenetics Knowledge and Attitudes of Primary Care Physicians in Manitoba (PGx-KAP)

Short Description of Research:

Pharmacogenetics (PGx) is the study of genetic variation in medication response both in terms of therapeutic and adverse effects. The ability to prescribe medication while limiting adverse drug reactions and promoting the best possible care for patients is an essential step toward patient-centred health and wellness. Pharmacogenetic testing has the potential to optimize medication therapy for individual patients. To inform the implementation of pharmacogenetic-supported prescribing of medications in Manitoba, it is vital to understand the facilitators and barriers from the perspective of physicians practicing in primary care. This study aims to understand the knowledge of and attitudes toward pharmacogenetic testing among physicians practicing in primary care within Manitoba. Physicians practicing in primary care will be invited to complete a brief, anonymous questionnaire to assess knowledge of and attitudes toward pharmacogenetic testing. Results from this survey study will be used to inform the future delivery of education and implementation of pharmacogenetics-supported care in Manitoba.

PROJECT #3

PI Name (Last, First):	**Lakowski, Ted**
PI Email:	**Ted.Lakowski@umanitoba.ca**
Please advertise to students on my behalf: (yes/no)	**Yes**
I will approach a student myself: (yes/no)	**Yes**

Project Title: The enzymatic activity and inhibition of DOT1L for the treatment of childhood leukemia

Short Description of Research:

Mixed Lineage Leukemia is a childhood cancer that is difficult to treat and has a poor prognosis. It is caused by overexpression of the oncogene Homeobox protein A9 (HOXA9). The lysine methyltransferase (KMT) DOT1L methylates histone H3 at K79 (H3K79Me) in the HOXA9 promoter increasing its expression. Studies have shown that decreasing HOXA9 expression is sufficient to treat the disease. Inhibitors of DOT1L also reduce HOXA9 expression and are in clinical trials as a treatment for mixed lineage leukemia, however, initial results show that they have poor efficacy and dose limiting toxicities. DOT1L is active at multiple promoters, and we have shown that DOT1L inhibitors and drugs targeting epigenetic enzymes in general, alter the expression of many genes, likely leading to decreased efficacy and off-target effects. Therefore, to improve their efficacy and decrease adverse effects, the Lakowski Lab is developing DOT1L inhibitors that will be targeted to the HOXA9 promoter. In this project the student will recombinantly express and purify DOT1L, and then measure its activity and inhibition *in vitro*. Inhibitors in various phases of clinical trials will be tested in addition to broad spectrum methyltransferase inhibitors. The results will assist in the development of new inhibitors of DOT1L that are gene specific. Such inhibitors will be a new class of therapeutic for the treatment of Mixed Lineage Leukemia that will be more effective, while reducing required dose and toxicity compared to conventional DOT1L inhibitors.

PROJECT #4

PI Name (Last, First):	**Kowalec, Kaarina**
PI Email:	**Kaarina.kowalec@umanitoba.ca**
Please advertise to students on my behalf: (yes/no)	**Yes**
I will approach a student myself: (yes/no)	**No**

Project Title: Pharmacogenomics of dimethyl fumarate-induced lymphopenia in multiple sclerosis (MS)

Short Description of Research:

Over 20 disease-modifying therapies are approved for use in relapsing-onset or progressive MS; all provide some benefit, although none have been shown to halt the disease and all carry potential risks. The commonly used, first-line oral drug, dimethyl fumarate (DMF), has been associated with devastating infections. The prevention of opportunistic infections is essential to maintain DMF as a viable therapeutic option for MS. Currently, there are few clinically useful predictors of serious infections in persons with MS who are considering initiating DMF. Lymphopenia is a risk factor for the subsequent development of secondary infections in persons taking DMF. Regular screening of lymphocyte counts remains the main strategy in clinical practice, however, this does not predict, or prevent lymphopenia. Pharmacogenetics, the study of how genetic variation impacts drug treatment, may be the key to identifying who is at greatest risk of DMF-induced lymphopenia. The goal of our study is to identify genetic variation associated with DMF-lymphopenia, which can then be used to identify who is at the highest risk for experiencing this adverse reaction.

Overall aim*:** Investigate the polygenicity of DMF-lymphopenia in persons with MS. Hypothesis: Polygenic risk scores will stratify individuals into 'higher' and 'lower' risk for DMF-lymphopenia. ***Aim 1a: Develop a polygenic risk score for DMF-lymphopenia using a clinical trial cohort and assess its performance in a Canadian MS clinic cohort. ***Aim 1b:*** Determine whether (1) MS disease polygenic risk score or (2) absolute lymphocyte counts polygenic risk score are associated with DMF-lymphopenia in the Canadian cohort.

PROJECT #5

PI Name (Last, First):	**Marzban, Lucy**
PI Email:	**lucy.marzban@umanitoba.ca**
Please advertise to students on my behalf: (yes/no)	**Yes**
I will approach a student myself: (yes/no)	**No**

Project Title: A new pharmacological strategy to target protein aggregation in the pancreatic islets of diabetic patients to preserve insulin producing beta cells

Short Description of Research:

Diabetes is the most common endocrine disorder worldwide. Two major types of diabetes are Type 1 (T1D; Juvenile onset) and type 2 (T2D; adult onset) diabetes. In both types of diabetes pancreatic islet beta cells fail to produce enough insulin, leading to elevated blood glucose but the underlying mechanisms are different. T2D is caused by progressive beta-cell dysfunction and peripheral insulin resistance leading to relative insulin deficiency, whereas T1D is caused by destruction of beta cells by the body's immune system leading to lifelong insulin therapy. Islet transplantation has provided a feasible approach for treatment of T1D but is currently limited by low number of available pancreatic donors and short-term survival of transplanted islets.

Formation of toxic protein aggregates, named islet amyloid, is one of the important factors contributing to progressive beta-cell dysfunction and death in patients with T2D and islet graft failure in patients with T1D. Studies in our group focus on exploring the mechanisms by which amyloid causes islet beta-cell death and develop new therapeutic strategies to protect islets from amyloid toxicity thereby preserving beta-cells in patients with T2D and islet graft recipients with T1D. This summer project focuses on examining a new therapeutic strategy to target the formation of amyloid (protein aggregates) in pancreatic islets in diabetes. Students who join our research group will learn how to culture islets, prepare islet sections, immunolabel live and fixed cells/tissues, and use imaging techniques. Students will also develop problem-solving, data analysis, and presentation skills by participating in our regular lab meetings.

PROJECT #6

PI Name (Last, First):	**Labouta, Hagar**
PI Email:	**Hagar.labouta@umanitoba.ca**
Please advertise to students on my behalf: (yes/no)	**Yes**
I will approach a student myself: (yes/no)	**Yes**

Project Title: Bioinspired nanoparticles for breaching the biological barriers

Short Description of Research:

Nanotechnology, or more appropriately nanoscience, is a multidisciplinary branch of science that currently receives a lot of attention from researchers in the pharmaceutical and biomedical fields. Using nanoparticles in drug delivery and diagnostics offers several advantages over traditional formulations, such as modified pharmacokinetics and tissue distribution, site-specific targeting, reduced toxicity, prolonged release, improved stability and bioavailability. My research program aims at understanding the interaction of nanoparticles within the different biological compartments and translating this knowledge to design new generations of bio-inspired nanoparticles for breaching the biological barriers of the body. The student will be involved in a cutting edge research program to design various nanoparticles with different size, composition and surface properties. The student will then test these particles using in vitro cell models developed in the lab for therapeutic applications. The student will work in a collaborative environment among a team of researchers with different backgrounds who will guide him/her in his summer research project. The student will also attend lab meetings and will present his or her work to the team. Depending on the student's progress and contribution to the project, they can be a co-author on the outcome publication.