Summer Student Research Program  
Project List 2019

List updated: January 31, 2019

***Please keep checking the website as this list may be added to until the deadline***

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Supervisor(s): Dr. Larry Lynd (Director, Collaboration for Outcomes Research and Evaluation; Professor, Faculty of Pharmaceutical Sciences)

Project Title: The impact of a genetic diagnosis on the health outcomes of patients with suspected genetic disorders: A systematic review

Project Description: Genetic diseases affect approximately 5% of the population, and include an estimated 6,000 – 8,000 rare single-gene disorders. While some conditions have a distinctive clinical presentation and are best diagnosed with targeted testing, the majority of genetic disorders can be difficult to diagnose because many share common clinical features. For example, intellectual disability (prevalence of 1-2%) has been linked to mutations in more than 700 different genes. Broad-based genomic tests, including chromosomal microarray analysis (CMA), exome sequencing (ES), and whole-genome sequencing (WGS), which interrogate genetic variants across the whole genome, are increasingly being used to facilitate etiologic diagnosis of suspected genetic disorders. These powerful new technologies yield a much higher rate of diagnosis than alternative diagnostic tests, but are also more costly than existing tests. Moreover, the impact on health outcomes for patients who received a diagnosis is difficult to quantify due to the heterogeneity of the cohorts who receive these tests and the paucity of causal treatments for rare diseases. To inform ongoing economic evaluations of diagnostic genome-wide sequencing tests, we will conduct a systematic literature review of studies reporting on the impacts on patient care and health outcomes of receiving a genetic diagnosis via broad-based genomic tests.

Project Objectives: This systematic review will identify and evaluate all existing publications that report on the consequences for patient care and impact on health outcomes of diagnosis by CMA, ES, and WGS. The goal of the review is to summarize the evidence on health impacts, including changes in drug utilization, the rate of treatable conditions, treatment modalities, effects on mortality, morbidity, or quality of life, and other changes to patient care.

Project Activities: The project will involve: 1) conducting background research to identify appropriate literature and data sources; 2) developing a search strategy; 3) designing the search terms used in queries; 4) screening individual studies for inclusion; 5) summarizing and abstracting included studies; 5) evaluating the quality of included studies; 6) documenting the methodology used to conduct the reviews; and 7) outlining a manuscript reporting on the systematic review. The student will provide input at all stages of the project, and will work closely with the study team to design a search and evaluation strategy. Once the methodological approach for the reviews is established, the student should be able to work with minimal direct supervision under these guidelines while exercising sound judgment on when to refer problems to the supervisor. The student will be offered co-authorship on the publication that reports the results of the systematic review.
Summer Student Research Program Project Description
SSRP-Lynd-02

Supervisor: Dr. Larry Lynd (Director, Collaboration for Outcomes Research and Evaluation; Professor, Faculty of Pharmaceutical Sciences)

Project Title: Economic Evaluation of Gene Therapy Products: A Systematic Review

Project Description: Gene therapies use a diverse range of methods to modify gene expression or repair pathogenic genes in an individual patient. To date, at least 13 gene therapies have received marketing authorization worldwide, including five in the United States and one in Canada. They include treatments for ultra-rare single-gene disorders like adenosine deaminase deficiency–severe combined immunodeficiency (ADA-SCID) as well as oncolytic virus and chimeric antigen receptor T-cell (CAR-T) therapies for advanced cancers. A large number of additional gene therapies are being developed, including gene therapies for common diseases (e.g., age-related macular degeneration). While the cost of gene therapies is high (more than $1,000,000 per patient in some cases), leading to concerns about the budgetary impact of gene therapies for Canadian health systems, proponents of gene therapies have argued that a high-cost one-time treatment may be more cost-effective than existing drug therapies (e.g., enzyme replacement) that require ongoing treatment for life. However, economic evaluation of gene therapy products poses distinct challenges, such as small clinical trial sample size, uncertainty about the durability of the gene therapy’s effect, and costing the ancillary healthcare services required for the safe delivery of genetically modified cell-based therapies. To inform the rigorous evaluation of gene therapies in a Canadian context, we will be conducting a systematic literature review of existing economic evaluations of gene therapy products.

Project Objectives: This systematic review will identify and evaluate all existing publications that report on the cost-effectiveness and budgetary impact of gene therapy products. The goal of the review is to summarize the evidence on the cost-effectiveness of gene therapies as well as to identify common methodological weaknesses and challenges encountered when evaluating gene therapy products.

Project Activities: The project will involve: 1) conducting background research to identify appropriate literature and data sources; 2) developing a search strategy; 3) designing the search terms used in queries; 4) screening individual studies for inclusion; 5) summarizing and abstracting included studies; 5) evaluating the quality of included studies; 6) documenting the methodology used to conduct the reviews; and 7) outlining a manuscript reporting on the systematic review. The student will provide input at all stages of the project, and will work closely with the study team to design a search and evaluation strategy. Once the methodological approach for the reviews is established, the student should be able to work with minimal direct supervision under these guidelines while exercising sound judgment on when to refer problems to the supervisor. The student will be offered co-authorship on the publication that reports the results of the systematic review.
**Supervisor:** Brent Page

**Project Title:** Developing new anti-cancer therapies using state of the art chemical biology techniques

**Project Description:** Two projects are available that are focused on the design, synthesis and preliminary testing of novel chemical compounds to target dysfunctional signaling networks in cancer cells. Both projects have evolved from high-throughput screening campaigns and have employed state of the art chemical biology techniques including cellular thermal shift assays (CETSA), thermal proteome profiling (TPP), fluorescence tagging and others. Compounds that are synthesized within this project will be analyzed for their ability to bind specific targets in cancer cells and for their ability to halt the growth and proliferation of cancer cells using the latest models and technologies.

Summer students will gain exposure to a breadth of topics in drug discovery and development within these projects and will learn the basics of medicinal and organic chemistry (including synthesis and characterization of new compounds), chemical and cell biology techniques (including CETSA and cell proliferation assays), and will interact with a network of collaborators who will further assess the anti-cancer activity of newly synthesized compounds.

*Up to 2 positions are available.*
Project Title: Rheumatologists' Perceptions Regarding Barriers in the Implementation of Preventative Therapies in Rheumatoid Arthritis

Supervisor: Dr. Mark Harrison

Background: Rheumatoid arthritis (RA) is thought to develop through a process of “multiple hits”, involving genetic and environmental risk factors, followed by antibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), that accumulate during an “at-risk” pre-clinical phase. Increasingly, it is thought that the pre-clinical phases of the disease might offer a window of opportunity to identify those at risk and to offer potential preventive treatment. It is unclear whether rheumatologists would offer preventative treatment to asymptomatic patients highlighting a need to understand physicians’ perceptions of particular barriers in the implementation of preventative therapies in RA, that would need to be overcome before such therapies could be implemented.

Project Overview: The proposed SSRP project is part of a research program on acceptability and preferences of preventative treatment for RA in patients and rheumatologists. The objective of this project is to examine rheumatologists’ perceptions of barriers in the implementation of preventive therapies for RA. Prior work on this topic conducted a quantitative assessment of associations between perceptions of potential barriers and respondents’ characteristics, such as age, sex, ethnicity, years in practice, type of medical practice, and province. Building on this prior work, the objective of this project is to 1) conduct condensed literature reviews on the existing evidence on the most frequently cited barriers, and 2) obtain a deeper understanding of rheumatologists’ perspectives of these barriers by applying a qualitative research approach to previously conducted focus group interviews.

Project activities: This project will involve the student in the following activities:
1) Condensed literature review:
   - Perform literature searches and reviews pertaining to each perceived barrier
   - Assist with developing a synthesis strategy of the scientific evidence
   - Assist with summarizing and abstracting relevant literature
2) Qualitative content analysis of focus group transcripts:
   - Assist with conducting analysis of transcribed physician focus group interviews
   - Code and/or label concepts related to perceived barriers
   - Assist with constructing categories and subcategories or groupings and organize codes into higher level themes
   - Abstract themes and/or interpret relationships between constructed categories
   - Summarize constructed themes and categories into appropriate tables and where relevant, figures, with supporting quotes
**Expected outcome:** This project will contribute an overview of the evidence and a better understanding of physicians’ perceptions of barriers relating to the implementation of preventative therapies in RA. Results have direct implications for knowledge translation and program planning as the paradigm of RA changes from treating to preventing the disease over the next decade.

**Role of the Summer Student:** The summer student will work closely with the supervisor and research team to complete the project. The summer student will be responsible for conducting condensed literature reviews, qualitative content analyses of transcribed focus group data, and reporting of results. Excellent verbal and written and inter-personal communication skills are a prerequisite. Coursework in research methods and/or previous experience with qualitative data analysis is an asset. Must be detail-oriented, organized and self-motivated. The student will be offered co-authorship on publications of the results of the project.
Project Title: “Learning Scripts” in Pharmacy Education Settings

Supervisor: George S Pachev, Natalie E LeBlanc, Office of Educational Assessment

Project Description:

Goal
This study is to identify, through individual and group interviews with pharmacy students, the routine events and actions related to effective learning and to compare them to the “learning scripts” in experiential education settings, identified in a previous study.

Background
The notion of “script”, as introduced by Schank & Abelson\(^1\), denotes mental representations of routine everyday events, consisting of actions leading to a goal and related through spatial and temporal relations, rather than logic category relations. The presence of such representation helps understand everyday situations and provides “cognitive economy” by guiding expectations and actions.

In a recent study\(^2\) of pharmacy students’ learning during practicum, a script-like structure seemed to underlie the descriptions of learning situations. Common elements of this script included: a “trigger”, which could be a preceptor assigned task, or independently set goal by the student; an iterative process of “practice” involving preparation, looking up necessary information, application of the skill, reflection-in-action, self-assessment and looking for feedback or assessment; in some cases there is “follow up” and/or “reflection-on-action”. Conditions for effective learning when enacting this script include preceptor’s support, clear delineation (and acceptance by the student) of responsibilities, sense of independence, initiative and involvement in interaction with patients.

It is not clear whether “learning scripts” could be found in descriptions of learning in academic settings, and if similar structures were identified, how do they compare to the scripts in practicum settings. The study will explore these issues, guided by the research questions below.


Research questions
How do pharmacy students describe the situations, events, and action routines when they learn most effectively in academic settings? What are the associated conditions necessary for learning to occur? What are the preparation and/or follow-up activities needed to consolidate learning, if any?

Project activities
This project will involve the student in the following activities:
1. Literature review: searching the scholarly literature on the “script” concept and its application to education and in health sciences. Complete a written review of the literature.
2. Data collection: design data collection protocols; pilot the instruments. The successful candidate will gain experience in the development and administration of qualitative interviews and analyses of qualitative data.
3. Ethics approval: preparing documentation for submission to the Institutional Research Ethics Board, including letters of initial contact and consent forms.
4. Dissemination of results: creating and developing a poster and seminar for presentation to the Faculty and other audiences, and participating in the preparation of a manuscript suitable for publication.

The student undertaking this project will be expected to work effectively within general guidelines but with minimal direct supervision and to have excellent verbal and written communication skills.
Summer Student Research Program Project Description
SSRP-Ross-01

Project Title: Development of an *in vitro* model of Lipoprotein Lipase Deficiency (LPLD) to investigate the therapeutic efficacy of CRISPR/cas9 genome editing.

Supervisor: Dr. Colin Ross

Project Description

**Background:** Genome sequencing has aided our ability to understand and diagnose genetic diseases and cancer. However, less than 5% of human genetic diseases have approved treatments. LPLD is a rare autosomal recessive disorder, which affects the body's ability to metabolize fats. Previously, Dr. Ross helped develop a gene therapy for LPLD known as Glybera, which aimed at treating the genetic diseases by inserting functional copies of the LPL gene into patients. While this approach was successful and gained clinical approval, critical limitations remained.

**Project Overview:** To overcome these limitations, we are investigating the potential of using novel CRISPR/cas9 gene editors to directly repair a pathogenic mutation in the DNA sequence of the LPL gene. In order to evaluate and later optimize this novel approach, we are developing an *in vitro* disease model.

**Methods:** This project will require UBC biosafety and chemical safety training. The project involves lab-based molecular biology techniques, imaging, and bioinformatics-based analyses. Students will learn mammalian cell culture techniques, cloning techniques and analysis of enzymatic assays. In addition, the project will require quantitative data analyses and the application of statistics to summarize laboratory findings. Finally, the project will require detailed presentations of findings in weekly lab meetings and reporting of project findings.

**Role of the Summer Student:** The summer student will work closely with the supervisor, research associates/postdoctoral fellows and graduate students to complete the project. The research will involve significant laboratory-based research involving bacteria and mammalian cell lines. The role of the summer student will be to generate *in vitro* models of LPLD using cloning and transfection techniques. In addition, the student will use CRISPR/cas9 to correct the mutation and compare enzymatic activity to the wildtype levels. This exciting summer project will demonstrate proof-of-principle gene correction and will be the foundation for the development of a subsequent patient cell line model and *in vivo* mouse model. The summer student will be expected to participate in weekly lab meetings and prepare a final report and poster presentation.
Project Title: Optimization of novel strategies for therapeutic genome editing using *in vitro* and *in vivo* reporter model.

Supervisor: Dr. Colin Ross

Project Description

Background: Genome sequencing has aided our ability to understand and diagnose genetic diseases and cancer. However, less than 5% of human genetic diseases have approved treatments. Previously, gene therapies have focused on the treatment of genetic diseases by inserting functional copies of a gene into patient cells. While this approach has been successful, critical limitations remain.

Project Overview: To overcome these limitations, we are investigating the potential of using novel CRISPR/cas9 gene editors to specifically repair pathogenic mutations directly in the DNA sequence of the gene of interest. In order to optimize this novel approach, we are developing *in vitro* and *in vivo* reporter model systems that utilize the GFP and luciferase genes to evaluate nanotechnology-based approaches to deliver therapeutic components into cells.

Methods: This project will require UBC biosafety and chemical safety training. The project involves lab-based molecular biology techniques, imaging, and bioinformatics-based analyses. Students will learn mammalian cell culture techniques, fluorescent imaging, luminescence assays and flow cytometry. In addition, the project will require quantitative data analyses and the application of statistics to summarize laboratory findings. Finally, the project will require detailed presentations of findings in weekly lab meetings and reporting of project findings.

Role of the Summer Student: The summer student will work closely with the supervisor, research associates/postdoctoral fellows and graduate students to complete the project. The research will involve significant laboratory-based research involving bacteria and mammalian cell lines. The role of the summer student will be to generate *in vitro* reporter models and perform optimization experiments to improve gene editing efficiency. In addition, the summer student will assist in the further development of the *in vivo* mouse models by developing and conducting genotyping assays. These important foundational experiments using the cell lines will be applied to all subsequent disease models and *in vivo* mouse studies in the future. The summer student will be expected to participate in weekly lab meetings and prepare a final report and poster presentation.