RESEARCH SCHOLAR PROGRAM – 2018

SUPERVISOR & PROJECT INFORMATION FORM

Please complete and return, via email only (crems.programs@utoronto.ca) by *November 3rd 2017* .

Supervisor Information

Name: *Geoffrey Liu*

Email: *Geoffrey.Liu@uhn.ca*

Degree: *MD*

SGS Appointment (IMS, IHPME, LMP etc..):

Full SGS appointments in Medical Biophysics

and Epidemiology (Dalla Lana School of Public Health)

Academic Rank: *Professor (Full)*

Field of Research: *Oncology*

Research Institution Affiliation: *Princess Margaret Cancer Centre / Ontario Cancer Institute / Dalla Lana School of Public Health*

Allocation of student contact time (number of hours per week YOU are available to the student for any concerns or to review progress):

2-3 hours per week during academic year and 6 hours per week during each summer, all for 1:1 discussion of research project with Dr. Liu. In the summer, there will also be 2 hours of didactic teaching/seminars per week (see www.uhncombiel.com) co-led by Dr. Liu and Dr. Xu (Associate Professor, biostatistician). This is high priority research as we have received funding through a $12million US NCI U19 Collaborative Grant where we are one of four screening programs being used to study and validate biomarkers and predictive models (the others are: US NLST, Danish NELSON study, the UK Liverpool screening study). I have allotted 3 calendar-months (or 25%) or my research efforts into this study for the next two years.

In addition for each summer, there will 1 hour/day in the summer and 1 hour/week for teaching and discussion of research projects with our education coordinator, Cathi Brown, and additional scheduled time for biostatistical advice 1:1 with our COMBIEL biostatistical team. This team will be further backed by Maureen McGregor, the long time (>12 years) clinical coordinator for the Early Detection of Lung Cancer Screening Program, and Drs. Heidi Roberts (Professor) and John Kavanaugh (Assistant Professor), radiologists at the University Health Network who are the clinical radiological leads for this screening program.

Project Information

Title: **The Princess Margaret (PM) Lung Cancer Screening Program Biomarkers Project**

Description:

Since 2004, a lung cancer computed tomography (CT) screening research program at PM has been ongoing, recruiting over 5200 at-risk ever-smokers with at least 10 pack-years of smoking to variable lengths of time in between CT screening. Since 2005, serial blood sampling (plasma, serum, whole blood) has taken place at each CT screening visit. In a subset of over 2000 Toronto participants, detailed epidemiologic data, spirometry, and 2-D radiomic data have been collected. It is this wealth of data that has led this study to be selected, alongside the US National Lung Screening Trial (NLST), The Danish NELSON study, and the UK Liverpool Study, to be part of a large US National Cancer Institute-funded collaboration for cross-validating biomarkers of early detection and predictive models; unlike these other studies, long term screening of over a decade has taken place in many individuals. The student will be intimately involved in the preparation of datasets, participate in the cleaning of data, be involved with wet-laboratory biomarker evaluation, and perform statistical analysis in either SAS or R. Hence, proficiency and strong interest in obtaining quantitative analytical skills is a requirement for this project.

The CREMS research scholar will participate and lead in answering such research questions as: (a) Are the incidence rates of lung cancer stable, increasing, or decreasing with long term screening? We are the only study in the collaborative group to have long term screening data; (b) What is the additional benefit of adding *BRM* polymorphisms to the current clinical predictive model for lung cancer (the Tammemagi model)? These germline polymorphic variants were discovered to be associated with a doubling of lung cancer risk in my group; (c) What are the detection limits of cell-free global methylome and genomic analysis of DNA in serial screening plasma samples for lung cancer? At PM, several of our collaborators have developed novel early detection biomarker platforms that can not only identify cancer in plasma, but also the cancer site and histological subtype of cancer through bioinformatic pattern recognition. If interested, the CREMS research scholar can also develop his or her own research question from this large and currently untapped database. The analysis of a primary research question (likely either (a) or (b) or one developed by the scholar), led by the scholar, will be submitted for international presentation, and a manuscript submitted for publication. The methodological training is designed to promote the development of the scholar towards performing future, independent research. The student will become integrated into the Cancer Outcomes, Medicine, Biostatistics, Informatics, Epidemiology, and Laboratory Medicine research training program (COMBIEL – www.uhncombiel.com), and where appropriate, will also be exposed to other trainees in CIHR training programs in Molecular Pathology (www.molecularpathology.ca), Genetic Epidemiology (www.stage.utoronto.ca), and Radiation Oncology (http://www.radonc.utoronto.ca/stars21) in relation to precision oncology, and screening biomarker research.

If human subjects are involved, have Ethics been obtained?

☒YES ☐NO ☐Application Submitted ☐N/A

All existing and planned projects have REB approval.

Do you expect this work will be published within the 20 months?

☒YES ☐NO ☐Uncertain

Every past CREMS Research Scholar in our laboratory has published at least one manuscript by the end of the research period, and the range is 3-6 in total over the course of the entire medical school period. A current Research Scholar in his 10th month this year has two manuscripts in preparation, one American Society for Clinical Oncology abstract submitted, and two in preparation.

Student's roles and responsibilities

Please indicate who will serve as the student's direct report (PI, PhD student,

technician etc…)

Because of the intense nature of the CREMS Research Scholar program, the student will report directly to Dr. Liu, supported by Cathi Brown, a MSc. level epidemiologist, and Wei Xu, a genetic and trials PhD biostatistician. The scholar may also obtain study design and implementation help from other members of the laboratory. (see figure).

Scholar's Roles and Responsibilities will be similar to former successful CREMS Research Scholar roles/responsibilities of Drs. Naik, Eng, and current medical student Lee. Note that Drs. Naik and Eng, both past 20-month CREMS research scholars, have won (between them) six American Society of Clinical Oncology Merit Awards, two Novartis Oncology Young Canadian Investigator Awards, and a CIHR ICR Publication Prize for their CREMS-related research projects. Although Dr. Liu has a current Research Scholar, the time-limited opportunity as a result of this new funded grant does not overlap with any of Mr. Lee's projects.
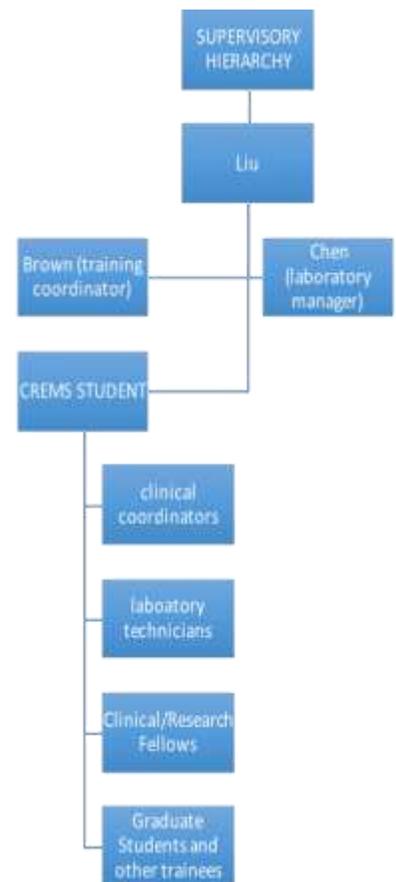
(1) *January, 2018: The CREMS scholar will obtain appropriate ID and research training as required by University Health Network (UHN) to access Electronic Patient Records, Patient Scheduling System (PHS), clinical research training certificate (required of all research personnel), and complete all administrative forms to become student UHN employee, with VPN laptop access. Cathi Brown and Zhuo Chen will guide this process.*

(2) *January-April, 2018: The CREMS scholar will become familiar with the existing dataset and study components, immersing himself or herself with understanding the many components of this research program, in order to be able to eventually develop a research question through to analysis and publication.*

(3) *January-April, 2018. The CREMS scholar will brush up on their SAS or R analytical skills (basic SAS or R training is a prerequisite for this student!)*

(4) *January-April, 2018. The CREMS scholar will perform the requisite literature search to become familiar with lung cancer screening research. This may be branched off into a systematic review manuscript, if the student has time, but will form the basis of development of the research question. Direct supervision by Dr. Liu and Cathi Brown.*

(5) *May-August, 2018. The CREMS scholar will focus on data merging, cleaning, and initial analysis, while finalizing his statistical analysis plan. Note that because this is a longstanding research program, REB amendments are not necessary; however, the scholar will sign the delegation log to become a member of the study team. (Liu/Brown)*

(6) *May-August, 2018. The CREMS scholar will be an integral member of the summer COMBIEL training program, and is expected to lead at least one or two undergraduate or medical undergraduate students who will help verify data and clean data. The scholar is expected to work with our COMBIEL statistics team (led by Dr. Xu) to finalize the SAP (Statistical Analysis Plan).(Liu/Brown/Xu)*

(7) *July-August, 2018. CREMS scholar will expose himself to all laboratory aspects of biomarker development pipeline performed in the Liu laboratory, including discovery, validation, clinical utility, and ELSI (ethical, legal, societal implication) research (Liu/Chen).*

(8) *September 2018- May, 2019. The CREMS student will follow the SAP and run appropriate analyses, under the direct supervision of Drs Liu and Xu, and Cathi Brown. More complex modeling will be performed in conjunction with a Waterloo Biostatistical Intern funded by the Ontario Institute for Cancer Research, with Dr. Xu as supervisor; a different intern has been chosen to work in this capacity for the past 8 years (9 month placement).*

(9) *June, 2019-August, 2019. CREMS scholar will begin drafting the manuscript for publication and submit the data for presentation at a national or international meeting.*

(10) *2018-2019: Present at the U of T Undergraduate Medical Student Research Day.*

This is a special CREMS Research Scholar project. It requires a specific background of quantitative skills, but is expected to result in a unique opportunity for the right Scholar interested in Oncology, Disease Prevention and Early Detection, and/or Translational Biomarkers.