



RESEARCH SCHOLAR PROGRAM – 2018

SUPERVISOR & PROJECT INFORMATION FORM

Please complete and return, via email only (crems.programs@utoronto.ca) by **November 3rd 2017** (forms received after this date will not be posted).

Supervisor Information

Name: Stephen Juvet

Email: stephen.juvet@uhn.ca

Degree: MD PhD

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

IMS, Immunology

Academic Rank: Assistant Professor

Field of Research: Transplant immunology, immune tolerance, lung transplantation

Research Institution Affiliation (if applicable): Toronto General Hospital Research Institute

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

I will have approximately one hour per week for one-on-one discussions. I co-lead a lung transplant immunology research group (the CLAD Team) with my colleague Dr. Tereza Martinu, and the CREMS student will be a participant in this group. As such, there will also be 2-3 hours of lab meeting time each week for group discussions and feedback. In these meetings, students have regular opportunities to present and get feedback on their work.

Project Information

Title: Innate and adaptive immune activation during primary graft dysfunction in human lung transplantation

Description (max 500 words):

Lung transplantation is the only life-saving therapy for patients suffering from end-stage lung disease. Unfortunately, the lung allograft is susceptible to a range of inflammatory, infectious and alloimmune (anti-donor) injuries that begin in the donor and continue in the recipient and often culminate in fibrosis and late graft failure, known as chronic lung allograft dysfunction (CLAD). One of the most important early injuries is called **primary graft dysfunction (PGD)**. PGD is a form of acute lung injury with impaired oxygenation occurring in 15-20% of lung allograft recipients within 72 hours of transplantation. It can lead to mortality in its own right and an increased risk of CLAD in the long term.

Our laboratory is interested in understanding the immunological processes that underlie CLAD development. As a key CLAD risk factor, the mechanistic links between PGD and CLAD are incompletely understood. We are currently investigating these links in a murine model of lung transplantation, but exploring these relationships in human lung transplant recipients is also needed. We have developed an expertise in mass cytometry, a multidimensional cellular phenotypic profiling technique that allows examination of up to 40 cell-associated proteins in parallel. We have collected cryopreserved leukocytes on postoperative day 1 from 100 consecutive lung transplant recipients, which will provide us with an opportunity to explore immune cells and their activation states in patients with (n=10-20) and without PGD (n=20) in this cohort. Our hypothesis is that PGD patients will display distinct patterns of innate and adaptive immune system activation in the peripheral blood in comparison to patients without PGD.

In this project, the CREMS student will participate in all aspects of this translational research project. Over the course of the Research Scholar Program, the student will have the following objectives:

1. Collect relevant clinical data from the Toronto Lung Transplant Program database on the patients in the cohort including PGD classification, donor and recipient information, HLA data, subsequent rejection episodes and pulmonary function (*can begin in orientation period*).
2. With an experienced postdoctoral fellow in the group, develop and optimize the mass cytometry antibody panel that will be used to characterize the cryopreserved leukocytes from this cohort (*summer 1*).
3. Stain and process the samples for mass cytometric analysis at SickKids Hospital (*summer 1 – year 2*).

4. Analyze the data with respect to the primary clinical outcome (PGD) and prepare the results for presentation and/or publication (*year 2 – summer II*).

In taking on this project, the CREMS student will have the opportunity to apply cutting edge immunological techniques in lung transplant patients to generate new knowledge. The student will interact with basic scientists, graduate students, technicians, clinicians and clinician-scientists, and will develop a deeper understanding of the physician-scientist career path.

If human subjects are involved, have Ethics been obtained?

YES NO Application Submitted N/A

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

YES NO Uncertain

Student's roles and responsibilities (please be specific)

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

The specific objectives for the student are outlined above. The student is expected to obtain a general working knowledge of lung transplantation and its shortcomings, along with basic concepts of transplant immunology. He or she will gather information from an existing database. Working with the PI and a postdoctoral fellow with expertise in mass cytometry, the student will develop and test an antibody panel with relevance to PGD. Ultimately he/she will then apply that panel to the actual patient samples and relate the findings to the clinical observations. The student will also have access to help from research technicians and graduate students in the group.