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: Donna Wall

Email: donna.wall@sickkids.ca

Degree: MD

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

Academic Rank: Professor

Field of Research: Transplant immunology/hematopoiesis

Research Institution Affiliation (if applicable): SickKids 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): Flexible

We have weekly lab meeting on Wednesday afternoon but door is open. This is project will be linked closely with the pediatric BMT program – opportunity to be involved for both clinical and more basic research activities.

Project Information

Title: Impact of pre-transplant inflammation on the host hematopoietic stem cell susceptibility to the transplant preparative regimen.

Description (max 500 words):

Hematopoietic stem cell transplant is a potential life-saving treatment for malignant and non-malignant blood disorders. The process of allogeneic transplant involves replacement of host hematopoiesis with donor hematopoietic stem cells which go on to provide lifelong hematopoiesis. It can be difficult to achieve full donor engraftment in patients undergoing allogeneic transplant, full donor engraftment is desired as mixed chimerism can lead to graft failure and less effective graft versus leukemia effect. Achieving full donor engraftment is especially daunting in patients who are inflamed in the immediate pre-transplant period (e.g. patients with hemophagocytic lymphohistiocytosis or patients with infections). These patients will have high levels of inflammatory cytokines. There is evidence that inflammatory cytokines such as tumor necrosis factor alpha (TNFα) can affect cell cycle status and place/keep more of the hematopoietic stem cells in a quiescent state. It has been shown that quiescent cells are able to escape chemotherapy treatment and thus render these cells less susceptible to our pre-transplant preparative chemotherapy. The host hematopoietic stem cells that are "left behind" can then, post-transplant, compete with the donor hematopoietic stem cells for engraftment and subsequent hematopoiesis. This project will evaluate hematopoietic stem cells from normal subjects and patients pre-transplant for their ability to enter cell division and differentiate in the absence/ presence of inflammatory cytokines. There will be complementary evaluations of transplant outcomes and cytokine profiles (obtained pre-transplant and before transplant preparative regimen is started) in patients undergoing transplant, comparing patients that were inflamed or non-inflamed pre-transplant. The obtained data can potentially lead to a change in pre-transplant preparative regimen for inflamed patients going into allogeneic hematopoietic stem cell transplant.

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 student will work under guidance of our research associate, Karin Hermans, in performing hematopoietic colony assays and detailed mass cytometry assays of cell proliferation and hematopoietic cell subsets in CD34+ cells isolated from normal cord blood/peripheral blood stem cells/bone marrow and compare those cells to patient samples obtained pre-transplant.

There will be an opportunity to assist in the chart review of the patients – evaluating clinical correlates of inflammation in the immediate pre-transplant period.

The clinical study is being led by Dr. Salah Ali, BMT/CT subspecialty fellow. REB application is in preparation. Pre-clinical trial work with normal cells can be started immediately.

The lab team additionally has 2 experienced technologists and we would look for opportunities for the student to learn basic flow cytometry, cell counting, quantitative PCR methodologies as well as the colony assays and CyTOF. There is currently another undergraduate student, 2 clinical post-doctoral fellows and scientist, Dr. Joerg Kreuger, working with the team.