

Supervisor & Project Information Form

Please complete and return via email ONLY to gdip.hres@utoronto.ca by **Monday September 30, 2019**

Supervisor Information

MUST have unrestricted SGS appointment (appointment to supervise graduate students)

Name: Donna Wall	Email: donna.wall@sickkids.ca
SGS Department: Immunology	Field of Research: Transplant immunology/hematopoiesis
Research Institution affiliation (if applicable): SickKids Research Institute	Location of Work: SickKids Research Institute
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 meetings on Monday morning, but door is open. This project will be linked closely with the pediatric BMT program – opportunity to be involved in both clinical and more translational/basic research activities.

Project Information (will be posted on GDipHR website for student access)

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 (TNF α) 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 the appropriate Research Ethics Board approvals been obtained?

Yes No Application Submitted (Date: _____)

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

Yes No Uncertain / Other

Student Roles & Responsibilities (please be as specific as possible)

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

The student will work under guidance of our research associate, Dr. Karin Hermans, in performing hematopoietic colony assays and detailed flow 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 lab team additionally has one experienced technician, one medical student, two undergraduate students, 2 clinical fellows and a project investigator working with the team.