Please complete and return via email only (gdip.hres@utoronto.ca) by September 4, 2018 (forms received after this date will not be posted).

**Supervisor Information**

**Name:** Donna Wall  
**Email:** donna.wall@sickkids.ca

**Degree(s):** MD  
**SGS Department:** 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 a weekly lab meeting on Wednesday afternoon but door is open. This project will be linked closely with the pediatric Bone Marrow Transplant/Cellular Therapy program – opportunity to be involved for both clinical and more basic research activities.
Project Information (for posting on GDipHR website)

Title: Myeloid-derived suppressor cells as a cellular checkpoint after hematopoietic stem cell transplant

Description (max 500 words):

Hematopoietic stem cell transplantation (HSCT) involves engraftment of donor hematopoietic stem/progenitor cells (HSPC) with subsequent life-long hematopoiesis in the recipient. Major complications include graft-versus-host disease (GVHD) and relapse of the underlying disease – both controlled by donor-derived immune reactivity against the host (GVHD) and/or the cancer (also known as graft-versus-leukemia (GVL)).

Early post-HSCT there is a massive expansion of young myeloid cells under conditions of tissue damage where they develop strong immunosuppressive features – defined as myeloid-derived suppressor cells (MDSC). In addition to the early post-HSCT setting, MDSC are expanded in cancer, autoimmunity, and chronic infections and are potently suppressive of effector T cell, natural killer, and dendritic cell number and function while enhancing other regulatory cell populations. To date the role of MDSC and their downstream effect on immune cells has been underappreciated as an important checkpoint in the GVL/GVHD balance.

This project will measure MDSC and other components of the innate immune system in a cohort of patients undergoing HSCT utilizing mass cytometry (CyTOF). We will leverage our earlier observations that fully functional MDSC recover early post-HSCT with a first time study of the dynamics of activation of all the early cellular elements in patients with and without GVHD/relapse – with the goal of identifying important interactions that set the stage for GVHD/GVL activity. The combination of recent intensive chemotherapy, rapid expansion of these early post-transplant cell populations sets the stage for a clinical trial that will inhibit down-regulatory elements and enhance anti-tumor cytotoxicity in an early phase clinical trial based on the results of the proposed studies.

By focusing on the early post-transplant myeloid compartment and/or the HSPC graft we will identify novel approaches to optimize GVL while minimizing GVHD. Further young MDSC hold the potential of being an important HSPC-derived cellular therapy given their broad ability to suppress both innate and cognate immune reactions – not only in the setting of transplantation but potentially across a range of autoimmune disorders.
If human subjects are involved, have the appropriate Research Ethics Board approvals 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 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 detailed mass cytometry (CyTOF) analysis and functional analysis of the hematopoietic stem/progenitor grafts.

There will be an opportunity to assist in the chart review of the patients – evaluating clinical correlates of graft composition and post-transplant outcome (Graft-versus-Host-Disease, relapse).

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 medical student and an undergraduate student, 2 clinical fellows and scientist, Dr. Joerg Krueger, working with the team.