PhD DEFENCE – Wednesday, December 10th

Student: Dana (Kyluik) Price

Title: **THE EFFECTS OF POLYMER-MEDIATED IMMUNOCAMOUFLAGE ON ALLORECOGNITION OF BLOOD CELLS**

Time and Location: 4:00 pm, Room 203, Graduate Student Centre, UBC Campus

Supervisor: Dr. Mark Scott

Abstract

Allorecognition initiates the adverse events of red blood cell (RBC) alloimunization and tissue rejection. Current clinical approaches utilize tissue matching (HLA and blood typing) and immunosuppressive agents to attenuate allorecognition. These practices, however, lead to inventory and drug toxicity issues. Immunocamouflage of cell surfaces by the covalent grafting of methoxypoly(ethylene glycol) (mPEG; PEGylation) has potential utility for prevention of allorecognition. Previous studies have demonstrated the efficacy of immune cell and tissue immunocamouflage both *in vitro* and *in vivo*. However, the use of alternative polymers and the consequences of surface modification during allorecognition events have not been fully defined. To this end, we compared the traditionally utilized mPEG, to a novel polymer species polyethyloxazoline (PEOZ) to explore the effects of polymer grafting to human RBC and leukocytes (WBC) on cell structure, function, viability, as well as allorecognition. PEOZ has attributes that make it an attractive alternative to mPEG, and from a cellular bioengineering perspective, the low viscosity and decreased hydrophilicity of PEOZ could offer some biological and therapeutic advantages. Our studies showed that although PEOZ mediated significant immunocamouflage of cells, mPEG demonstrated improved efficacy in RBC studies. However, PEOZ would be useful for the immunocamouflage of cells, especially for patients that exhibit anti-PEG antibodies. Furthermore, we assessed the consequences of mPEG surface modification to WBC interactions and intracellular events during allorecognition. Our results demonstrated significant camouflage of surface proteins; decreased cell interactions; reduced NFκB activation, which resulted in decreased inflammatory cytokines such as IL2 and IL2Rα expression; and minimal effects to cell viability in modified cells during allogeneic challenge. The global camouflage of cells may decrease activation of numerous pathways and events responsible for cell proliferation during allorecognition. This makes PEGylation a viable non-toxic alternative to current immunosuppressive therapies. These findings demonstrated the therapeutic potential of both traditional mPEG and novel polymer alternatives. Furthermore, this work defined several mechanisms responsible for the decreased alloresponse of immunocamouflaged cells. Our results showed the clear potential for polymer-based bioengineering to modulate the immune response to allogeneic cells and would be useful for the prevention of allorecognition in transplantation and transfusion medicine.