



<b>Project Title: Inhibiting Inflammatory Bowel Disease</b>		<b>Code: SOMS7</b>
<b>Host School / Institute:</b> <a href="#">School of Medical Sciences/ Charles Perkins Centre</a>		<b>Address:</b> Charles Perkins Centre (Level 4 West; Redox Biology Lab)
<b>Certificates &amp; Clearances required:</b> No		
<b>Primary Supervisor:</b> <a href="#">Prof Paul Witting</a>		
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<b>Co-Supervisor/team:</b> Research Staff member: Dr Gulfam Ahmad		
<b>Project Type:</b> Laboratory based		
<b>Project Category:</b> Immunology & Infection		
<b>Skills / Attributes of a successful student:</b> Student should have the following attributes: 1) some previous experience working in a PC-2 lab; 2) background knowledge on immunology and inflammation; 3) some experience in biochemical and molecular procedures 4) happy to work with organs previously isolated from laboratory animals under Ethical approval.		
<b>Project Keywords:</b> inflamamtory bowel disease; drug intervention; nitroxide drug; bowel disorder		
<p><b>Project Description:</b> Inflammatory Bowel Disease (IBD) is a chronic condition typified by relapsing inflammation in the gastrointestinal tract (GI) often of idiopathic causes with limited therapeutic options. The overarching feature of IBD is severe bowel inflammation induced by an immune cell-mediated response. Corticosteroids therapy can control symptoms/flare-ups; however immunosuppressive side effects preclude long-term use. Steroid abuse is also implicated in onset/relapse and are contraindicated for GI disorders. Immunomodulating drugs (e.g., methotrexate) maintain remission and limit steroid dependency but exhibit major adverse effects. Anti-tumour necrosis factor (TNF) agents (e.g., Infliximab) are used for moderate to severe IBD with some success e.g., ~40% remission in ulcerative colitis (sub-type of IBD), however, infliximab fails to decrease GI complications, surgical rates and long-term treatment elevates risk of opportunistic infection. New innovative treatments for IBD are urgently needed to decrease dependency on immunomodulatory drugs currently in clinical use (1).</p> <p>The following aims are central to this project: Aim 1: Demonstrate that oxidants generated by MPO promote damage to the colon that is central to the pathogenesis of IBD and that cyclic nitroxides treatment inhibits this damage. Aim 2: Identify whether nitroxide drugs mitigate MPO-mediated damage in the inflamed colon in an adoptive transfer model of IBD?</p> <p>Outcomes generated in this study will inform on clinically relevant questions including:</p> <ul style="list-style-type: none"> <li>(i) Does MPO-mediated oxidant production in the inflamed colon influence immune pathways and if so,</li> <li>(ii) is MPO inhibition central to ameliorating IBD pathogenesis and</li> <li>(iii) Are cyclic nitroxides potentially a new class of MPO-inhibitors that are useful as a therapy for IBD?</li> </ul> <p>Student learning outcomes:</p> <ul style="list-style-type: none"> <li>i) gain a working understanding of IBD pathogenesis and understand how this translates to damage to the colon and symptomology in humans.</li> <li>ii) gain the necessary technical expertise to produce homogenised samples from isolated mouse colons for subsequent biochemical and molecular studies.</li> <li>iii) perform a series of biochemical and molecular studies related to identifying markers of inflammatory MPO-mediated damage.</li> <li>iv) Link the outcomes from studies identified in (3) above with clinical parameters that will be available via previous monitoring of animal behaviour during IBD active phase.</li> </ul>		