ImmunoTools IT-Box-Cy55M-Award 2013

Aoife Cannon

PhD Supervisor: Dr. Jacintha O'Sullivan

Dept. of Surgery, Trinity Centre for Health Sciences,
St. James's Hospital, Dublin 8, Ireland

Determining the molecular biology of the protective effect of smoking in Ulcerative Colitis

Ulcerative Colitis (UC) is a form of inflammatory bowel disease (IBD) that affects the gastrointestinal tract. The aetiology of the disease is largely unknown. Currently there is no cure for the disease and treatment involves the use of steroids and immunosuppressive drugs to control the symptoms. Interestingly, smoking confers a protective effect in UC. Clinically, it is well recognised that the severity of the disease is higher in UC non-smokers than smokers. However, the exact biological mechanism of this protective effect remains largely unknown. The aim of my Ph.D. is to elucidate the mechanism of the protection that smoking confers and to investigate the interaction of 2 novel biological compounds, identified from cigarette smoke, with the immune system.

Although the full pathogenesis of the disease is unclear, it is, however, known that the immune system plays a huge role in the development of the disease. Cytokines in particular are central to the pathways that take place in UC. Pro-Inflammatory cytokines such as IL-1β, IL-6, TNF-α and IL-13 have a critical role in the pathophysiology of UC. During the active states of the disease, the tissue and vasculature of the colon are disrupted. Hypoxia ensues and the hypoxia-sensitive transcriptional regulators Hypoxia-Inducing-Factor-1 (HIF-1) and Nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) are activated.

It has been shown previously in studies in mice that activation of HIF-1 is protective in IBD. By knocking out the NFκB pathway in a murine model, the mice had increased susceptibilty to chemically induced colitis, suggesting NFκB plays a protective role in UC. NFκB is activated by a number of inflammatory stimuli including cytokines and bacterial products.

We plan to use the dextran sodium sulfate (DSS) mouse model of colitis to analyse the cytokine expression profile in the mice. Experimentally, we will homogenise the colon and screen for levels of pro-inflammatory cytokines. Many of the cytokines from the Immunotools IT-Box-Cy55M will be used, including; IL-1β, IL-6, IL-10 ,IL-13 TNF-α, IL-17. The data this will generate will give us an insight into the immune profile of UC in a murine model which will in turn give us a greater understanding of the role of the immune system in the progression of UC.

ImmunoTools IT-Box-Cy55M for Aoife Cannon includes 55 recombinant cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF DETAILS