ImmunoTools *special* Award 2022

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Role of a gut pathobiont on nonsteroidal anti-inflammatory drug-induced inflammation and relevance to inflammatory bowel disease (IBD)

Background

Inflammatory bowel diseases (IBD) comprising Crohn's disease (CD) and ulcerative colitis (UC); are chronic inflammatory states of the gastrointestinal tract. The genetic make-up, the gut microbiota, the environment, and the immune response are believed to be responsible for the aetiology of the disease. Loss of tolerance to commensal enteric microorganisms is a hallmark of IBD, which leads to uncontrolled chronic inflammation. Genome-wide association studies (GWAS) have identified over 200 SNPs associated with IBD, including genes regulating the response to invading bacteria such as NOD2 and ATG16L1.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most common drug types used for the treatment of various inflammatory conditions. NSAIDs are often used by IBD patients for extraintestinal manifestations and non-IBD related conditions. Mucosal injury and ulcers are common adverse effects seen in NSAID users. Due to its inflammatory and ulcer-inducing properties, NSAIDs are believed to exacerbate inflammation in patients with IBD.

Inflammasomes are a family of multiprotein complexes that play a critical role in the innate immune response against bacteria. Bacteria are recognised by NOD-like receptors (NLRs). Upon recognition, NLRs interact with the adaptor protein ASC and caspase-1 to promote the maturation and secretion of pro-inflammatory IL-1β and induce a type of bacteria-induced cell death called pyroptosis via gasdermin D. A recent study has suggested that dysregulation of the inflammasomes contributes to the NSAID-induced inflammation in a pre-clinical mouse model.

Adherent-invasive *Escherichia coli* (AIEC) is a gut pathobiont that has been associated with the pathogenesis of IBD. We have preliminary data indicating that AIEC interacts with the inflammasome in macrophages and intestinal epithelial cells.

Objective

This project aims to examine whether AIEC-induced inflammasome and macrophage activation sensitise the host to NSAID-induced inflammation and ulcer formation.

For this purpose, we will use a mouse model of IBD. Mice will be infected with AIEC by oral gavage. After the infection, animals will be exposed to NSAIDs. We will access the levels of systemic and localised inflammation using pro-inflammatory cytokine ELISA on plasma and colon tissue homogenate, respectively. We will also characterise the macrophage activation profile by flow cytometry.

I will use the ImmunoTools mouse TNF-α and GM-CSF ELISA-set to gain insight into how IBD-associated bacteria sensitise the host to NSAID-induced inflammation. ImmunoTools FITC-CD11b, APC-CD11b anti-mouse antibodies will be used as a part of a flow cytometry antibody panel for the macrophage activation analysis.

ImmunoTools *special* AWARD for **Raminder Singh** includes 10 reagents

FITC - conjugated anti-mouse CD11b

APC - conjugated anti-mouse CD11b

mouse ELISA-set (for one 96 plate): TNF-α, GM-CSF

DETAILS more AWARDS