Inflammatory bowel diseases (IBD) are a spectrum of chronic and debilitating immune-mediated inflammatory disorders with multi-factorial pathogenesis. The usual course of disease involves periods of remission interspersed with occasional flare-ups. As there is no cure, the approach to treatment is symptomatic care following a step-up or step-wise approach, with new drugs being added until a response is achieved. Clinical remission is only achieved in a relatively small percentage of patients (usually less than 30%), highlighting the need for new therapeutic approaches.

Technology

- QIMR Berghofer researchers have discovered a novel mediator of inflammation. To keep the name of the target confidential it is referred to as Inflammatory Response Protein (IRP).
- IRP is expressed by different immune cells at distinct stages of Ulcerative Colitis (UC), providing an opportunity to selectively control inflammation depending on the stage of disease.
- Studies in gene-deficient mice have identified important roles for IRP in UC, and have validated IRP as a therapeutic target.
- The absence of IRP activity reduces blood concentrations of pro-inflammatory cytokines and also increases anti-inflammatory cytokines to effectively control an immune response. Therefore, unlike existing therapies such as anti-TNF mAbs, an anti-IRP mAb will have a dual mode of anti-inflammatory action.
- Although the initial focus is on IBD, we have an opportunity to also target other inflammatory diseases, where patients are under-served by current treatments, for example rheumatoid arthritis.

Market

Inflammatory bowel diseases (IBDs) are a lifelong disease that present at any age and have no known cure. They are emerging global diseases, but Australia already has one of the highest prevalence rates in the world. More than 75,000 Australians live with IBD, with numbers expected to surpass 100,000 by 2022. IBDs are more prevalent in developed countries, with over 1.5 million and 2 million people affected in Europe and USA, respectively. However, the incidence is rapidly increasing in emerging markets, in particular China, due to increased urbanization and industrialisation. The global IBD treatment market is expected to be worth $22.4 billion by 2026.
Targeting IRP via blocking its function using an antagonist antibody is a novel approach to dampening inflammation in IBDs. Competitive advantages include:

- Targeted treatment with reduced toxicity and adverse events, since IRP is not expressed by non-immune cells.
- Potential to identify patients that would benefit from an IRP monoclonal antibody treatment and tailor anti-IRP monoclonal antibody administration to IRP expression.
- Improved effectiveness by targeting multiple stages of disease pathology, including cellular recruitment, cytotoxic granule release and cytokine production by immune cells.

**Lead Researcher**

Christian Engwerda is a NHMRC Senior Research Fellow. He was a Postdoctoral Fellow at the University of Maryland (Baltimore, USA) for 3 years and then spent 8 years at the London School of Hygiene and Tropical Medicine (UK) as a Lecturer and Wellcome Trust Career Development Fellow. He moved to QIMR in 2003 and established the Immunology and Infection Laboratory as a NHMRC Career Development Fellow. He is Head of the Infectious Diseases Division and is an Honorary Professor at the University of Queensland. He holds a NHMRC SRF that commenced in 2019, is CI on a NHMRC Program grant (CI with 8 others) that commenced in 2018. He’s also a PI on a NIH-funded Tropical Medicine Research Centre (TMRC) grant (2017-22).

**Intellectual Property**

QIMR Berghofer has a PCT patent application on IRP directed to compositions and methods of treating or preventing an autoimmune disease, inflammatory conditions or cancer.

*Irp−/− mice are refractory to DSS-induced colitis*

*Irp−/− mice have minimal histopathological abnormalities compare to the wild-type (WT) mice*