Immune system reset by removal of autoreactive/pathogenic cells with leukocyte depleting monoclonal antibodies.

- Two novel antibodies targeting Th1 and Th17 cells.
- Near complete removal of pathogenic cells.
- Well validated targets in disease.

THE CHALLENGE

Autoimmune diseases, such as multiple sclerosis (MS), rheumatoid arthritis (RA), inflammatory bowel disease (IBD), type 1 diabetes (T1D), and psoriasis (Ps) are a heterogeneous set of diseases that share common hallmarks including multifactorial aetiologies, involvement of T cell-mediated autoimmune pathomechanisms, and a chronic clinical course that often requires lifelong disease management.

In developed societies, the burden of autoimmune disease is ever-growing. The NIH estimates more than 23.5 million Americans suffer from autoimmune disease, and the prevalence is rising.

New leukocyte subsets that drive chronic inflammation and autoimmune diseases have come to light in recent years. These include TNF-producing Th1 cells, IL-17-producing Th17 cells, IL-22-producing Th22 cells, as well as IL-17-producing innate cells including γδ T cells, invariant natural killer T cells and group 3 innate lymphoid cells. This diversity of leukocytes and related cytokines provides new opportunities for more targeted therapeutics that inhibit a narrower band of pathogenic cells or molecules. Blocking antibodies that interfere with TNF or the IL-23/IL-17 axis are excellent examples of this new knowledge translating to breakthrough medicines. Nevertheless, effective treatment approaches are still lacking for many patients suffering from chronic immune-mediated inflammatory diseases.

THE TECHNOLOGY

The Monash research team led by Prof. Charles Mackay have demonstrated that depletion of specific T-cell subsets involved in autoimmune and inflammatory diseases can lead to a remarkable inhibition of disease in mice.

Previous work in the Mackay laboratory identified CXCR3 as possibly the best marker for activated and memory/effector T cells, associated with Th1 type response (and its absence from most Treg cells). The research team have also characterised CCR6 as a marker for Th17 cells, involved in the pathogenesis of MS and Ps.

Numerous mAbs to mouse and human CXCR3, and human CCR6, have been generated. Several of these mAbs have been engineered to deplete activated/effector T cells, for either Th1 or Th17 responses, and are effective in diseases where such cells play pathogenic roles.

The anti-CXCR3 or anti-CCR6 depleting mAbs allow for an “immune system reset” i.e. the near complete removal of pathogenic cells through depletion.

THE OPPORTUNITY

We are seeking a partnership to advance the antibodies by testing in a range of experimental models and conducting formal pre-clinical studies.

References


Figure 1: Cytotoxicity of activated human NK cells (effector) against a mixture of hCCR6 and hCXCR3 L1.2 cells (target) by R6 (anti-CCR6); X3 (anti-CXCR3); R6 + X3 and BsAb.

Figure 2: Depleting anti-CXCR3 mAb inhibits MCD diet-induced steatohepatitis and liver fibrosis. C57BL6 mice were fed with control (left panels) or MCD diet (middle and right panels) for 5 weeks. Mice were treated with either isotype control antibody (middle panels) or a depleting anti-CXCR3 antibody. Representative images of H&E (top panels) and Sirius red staining (bottom panels) for liver sections. Less collagen deposition (bottom right panel).