Anti-CXCR3 monoclonal antibody

THERAPEUTIC: Inflammation & Immunity

Product Type	Therapeutic monoclonal antibody
Indication/ROA	Autoimmune diseases (Type 1 diabetes, graft versus host disease, inflammatory bowel disease, other) and metabolic disorders (NASH)
Target/MoA	C-X-C motif chemokine receptor 3 (CXCR3); ablation of pathogenic effector and memory immune cells expressing CXCR3 (mainly Th1 cells) using a depleting antibody
Development Stage	Lead optimisation, efficacy demonstrated
Brief Description & Differentiation	The chemokine receptor CXCR3 is a marker for effector and memory subsets in multiple different immune lineages including CD4, CD8, NKT, NK and B cells. Compelling evidence suggests that CXCR3 chemokine receptor plays a crucial role in the migration of pathological cells during the course of certain inflammatory diseases. Unfortunately, the use of two or more receptors by pathogenic cells may explain why targeting of individual chemokine receptors has proven disappointing in the clinic. • We have demonstrated that depletion of $CXCR3^+$ cells can lead to a remarkable inhibition of NASH in mice. • T cell depletion is a much more effective approach than mere blockade of the target. • The anti-CXCR3 mAbs allow for an "immune system reset" i.e. the near complete removal of pathogenic cells through depletion.
Research Team	Prof Charles Mackay and Dr Remy Robert
Intellectual Property	Provisional patent application covering method of use of CXCR3 depleting mAb in the treatment of fatty liver disease (in particular NASH) and other autoimmune disease (Filed Oct 2018). Lead anti-human CXCR3 mAb has not been disclosed and will be the subject of a new composition of matter patent application.
Key Publications	Confidential
Future	Demonstrate POC in multiple preclinical disease models. Progress to formal preclinical studies enabling human testing in phase 1a/b clinical trial.

➢ Key Data

Anti-mouse CXCR3 depleting mAb is remarkably effective in methionine-choline deficient (MCD) diet induced nonalcoholic steatohepatitis (NASH) model.

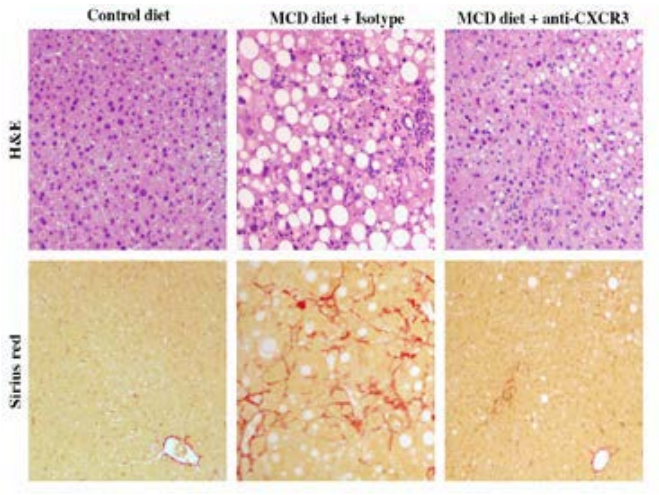

Figure 1: **Depleting anti-CXCR3 mAb inhibits MCD diet-induced steatohepatitis and liver fibrosis**. C57/BL6 mice were fed with control (left panels) or MCD diet (middle and right panels) for 5 weeks. Mice were treated with either isotype control antibody (middle panels) or a depleting anti-CXCR3 antibody. Representative images of H&E (top panels) and Sirius red staining (bottom panels) for liver sections. Less collagen deposition (bottom right panel).