



**CCRL2 : A New Chemokine Receptor**  
**anti-inflammatory target**

## **Programme Objective**

- Develop potent antagonists of the CCRL2 G-protein coupled receptor.
- To validate multiple indications for such molecules in a range of allergic and inflammatory disorders

## **Overview**

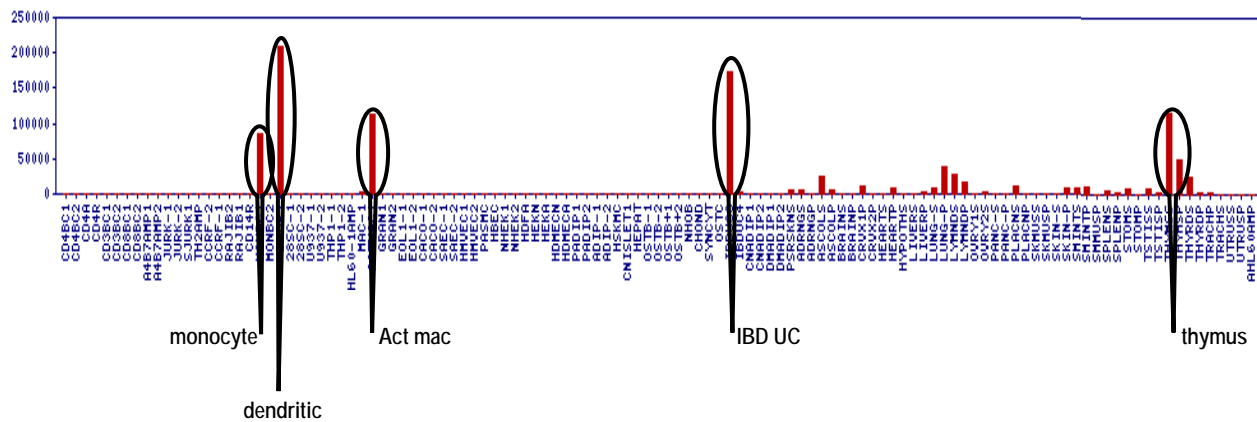
One of the GPCRs identified by Oxagen as genetically associated with a range of inflammatory diseases is the orphan C-C-chemokine receptor CCRL2. This receptor, also known as HCR, CRAM-A, CRAM-B, CKRX and Eo1 is found strongly expressed on macrophages and has an alternative spliced variant produced on activated macrophages. We have de-orphanised this receptor and shown that the major ligand for this receptor is the orphan chemokine MIP-4, also known as CCL-18, PARC, DC-CK-1 and AMAC-1. Many reports detail the putative roles of one or both of these biological molecules in the pathogenesis of rheumatoid arthritis, atherosclerosis, respiratory diseases, inflammatory bowel disease and allergic dermatitis.

## **Summary of CCRL2 observations**

- + CCRL2 is a chemokine receptor located on the cell surface of cells involved in immune response.
- + CCRL2 is implicated in multiple inflammatory conditions based on human genetic studies (Oxagen)
- + CCRL2 is predominantly expressed in monocytes, macrophages, and dendritic cells. A specific subset of CD4+ T-cells also express the receptor. Studies on the mouse receptor also indicate expression in Glial cells
- + A second splice variant of CCRL2, with an extended amino terminus, appears restricted in its expression to activated macrophages
- + Oxagen has de-orphanised CCRL2 and shown that CCRL2 binds the pro-inflammatory chemokines MIP4, MCP1, and MCP3. Activation of the receptor with these chemokines results in chemotaxis of recombinant CHO cells
- + These chemokines also drive chemotaxis of immune cells and are found in high concentrations at sites of inflammation in numerous inflammatory diseases



c) MIP-4 – Expression in monocytes, macrophage (activated and non-activated), IBD tissue and thymus.



### Programme Status

Oxagen is currently seeking partners to help us develop biologics and small molecule therapeutic agents which interfere with this receptor / ligand interaction and to explore their potential to treat a broad range of immune and inflammatory disorders.