ImmunoTools IT-Box-Cy55M-Award 2013

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Does strength of T cell receptor signalling regulate T helper-17 (Th17) responses in autoimmune arthritis?

T helper-17 (Th17) cells are an important T-cell subset involved in the pathogenesis of Rheumatoid Arthritis (RA) and other autoimmune conditions. Th17 cells are defined by the release of Interleukin-17 (IL-17) and, if targeted against joint components, can drive cartilage destruction and bone resorption. Our aim is to assess how the potency of signalling by the T-cell Receptor (TCR) influences the Th17 response using an array of peptide ligands. Critical to our work is the *ex-vivo* activation of T-cells by Bone Marrow Derived Dendritic Cells (BMDCs) presenting different peptides.

Recombinant proteins play a key role in this project allowing the differentiation of BMDCs using both rm GM-CSF and rm Flt3L to provide distinct Antigen Presenting Cell (APCs) populations for co-culture with purified $CD4^+$ T-cells. In order to assess the affect of different peptide ligands on T-cell differentiation a number of cytokines are used to modulate the environment during activation. These include Th1 (rm IL-2 and IFNγ), Th2 (rm IL-2 and rm IL-4), Th17 (rm IL-1β and rm IL-6) and iTregs (rm IL-2 and rm IL-10). It is important to fully characterise the effect on T-cell differentiation for each peptide across a range of cytokine milieus.

The diverse range of proteins will allow further characterisation of the helper T-cell responses in a number of cytokine environments and also distinct APC populations (rm GM-CSF vs. rm Ftl3L BMDCs vs. rm M-CSF derived Macrophages). These provide distinct T-cell populations that can be assessed for cytokine and surface marker profiles. Thus, permitting fuller characterisation with regards to how each peptide alters the propensity of Th17 cells to develop.

ImmunoTools IT-Box-Cy55M for Chris Tibbitt includes 55 recombinant mouse cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF

DETAILS