ImmunoTools IT-Box-Cy55M-Award 2013

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Friend Virus-induced Expansion of Two Unique Subsets of Natural Regulatory T Cells

Friend virus (FV) infection of mice induces the expansion and activation of regulatory T cells (Tregs) that dampen acute immune responses and promote the establishment and maintenance of chronic infection. Current results indicate that the responding Tregs are Helios$^+$ natural "nTregs" rather than induced "iTregs" converted from conventional CD4$^+$ T cells. Analysis of Treg TCR Vß chain usage revealed a broadly distributed polyclonal response, but with a disproportionate expansion of the Vß5$^+$ Treg subset. Vß5$^+$ Tregs are specific for an endogenous retrovirus-encoded superantigen (Sag), and the Vß5$^+$ Tregs displayed a unique phenotype. A marker of interest is TNF receptor 2 (TNFR2), as it was recently described to be important for Treg development and suppressive function. Interestingly, the blockage of its ligand TNFα leads to abrogation of the disproportionate expansion and activation of the Vß5$^+$ Treg subset, whereas the Vß5$^-$ Treg subset was not influenced. Thus the stimuli that drive Vß5$^+$ Treg expansion and marker expression during FV infection are different than the bulk population of Tregs. We would like to further investigate the need of different cytokines which can drive the induction of Sag and thereby the expansion of Vß5$^+$ Treg. We are also interested in the ways of induction of non-Vß5$^+$ Treg, as these are not virus specific but dependent on CD8$^+$ T cells. For this we will use an *in vitro* assay system and stimulate Tregs with different cytokines that are produced by different immune cells (CTL, dendritic cells, and macrophages) during FV infection to mimic the cytokine environment *in vitro*. This will help us to identify the critical cytokines. For this project it would be of great interest to use the *IT-Box-Cy55M* from ImmunoTools to do a screening of conditions that are important for Treg induction and especially expansion of Vß5$^+$ Tregs.

ImmunoTools *IT-Box-Cy55M for* **Jara Johanna Joedicke**

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