ImmunoTools IT-Box-Cy55M-Award 2013

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Influence of the mannose receptor on CD45 activity and T cell activation

The mannose receptor (MR) is a C-type lectin family member and is expressed by macrophages (MΦ) and dendritic cells (DC). DCs are part of the adaptive immune system and are able to induce an adaptive immune response by priming the differentiation, proliferation and activation of B and T lymphocytes. Several cell types like tolerogenic DCs or liver sinusoidal endothelial cells, which express high levels of MR, are able to induce T cell tolerance upon contact with T cells. Some studies report of a correlation of the MR with the induction of tolerance.

Recent studies identified the leukocyte common antigen CD45 as ligand for the MR on T lymphocytes. CD45 is expressed by all nucleated cell of hemopoietic origin and is required for antigen-induced T cell proliferation.

Recently, one member of the C-type lectin family, MΦ galactose-type lectin (MGL) was found to interact also with CD45 and thereby suppresses T cell activation. This was mediated by a reduction in CD45 phosphatase activity.

I investigate similar function of the MR on T cell activation. Especially, I focus on the influence of the MR during $CD4^+$ T cell differentiation.

The first step of this project is to differentiate freshly isolated murine $CD4^+$ T cells *in vitro* in a co-culture with MR-deficient DCs and a soluble recombinant MR construct.

The ImmunoTools *IT-Box-Cy55M* contains many recombinant cytokines (IL-2, IL-4, IL-6, IL-10, IL-27, MCP1/CCL2), which allows me to differentiate different subclasses of $CD4^+$ T cells. Afterwards, the ability of DCs to prime different subclasses of $CD4^+$ T cells will be analyzed by ELISA and CFC.

Another project of my PhD is the influence of secreted MR on DC function. Up to 20% of the MR is secreted by MΦ and DCs. This soluble form maintain its binding activity and could bind to CD45 on DCs. Recent studies indicate a role of CD45 in regulation of TLR-induces responses in DCs. Alterations of pro-inflammatory cytokines and IFN-β secretion in DCs was observed. Therefore, we hypothesized a tolerogenic function of the soluble MR on DC activity.

The recombinant cytokines of the ImmunoTools *IT-Box-Cy55M* would be used for immune-modulation experiments (IL-1alpha, IL-5, IL-13, IL-17, IL-21, IL-31, TNFα), especially to stimulate DCs. Thereby we could simulate different inflammatory conditions to investigate situations of enhanced MR sheeding. Furthermore, in consequence of immune responses alterations in cytokine profiles and surface marker regulation of DC will be analyzed.

ImmunoTools *IT-Box-Cy55M* for **Maria Embgenbroich**
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