ImmunoTools IT-Box-Cy55M-Award 2013

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Role of HDL components Apo AI and S1P in directing immune responses

High-density lipoproteins (HDL) possess atheroprotective functions which are associated to the ability of modulate membrane cholesterol content and to promote reverse cholesterol transport, favoring the transfer of cholesterol from peripheral tissues to the liver for excretion. Our group is investigating the role of HDL in modulating the immune response, by adressing their abilities to affect cholesterol bioavailability in the lipid rafts, membrane microdomains enriched in glycosphingolipids and cholesterol. Particularly, two main HDL components, the apolipoprotein AI (Apo AI) and sphingosine-1-phosphate (S1P), are critically involved in the modulation of immune responses.

The aim of our project is to study the role of these two molecules taking advantage of mice lacking Apo AI (Apo AI KO mice) and the S1P receptor 2 (S1PR2 KO mice), which is located on innate immune cells, particularly on monocytes/macrophages. Our purpose is to investigate the effects of the deficiency of these proteins on the polarization of specific immune cell subset following the use of specific cytokines from the ImmunoTools *IT-Box-Cy55* (the anti-inflammatory IL-4, IL-10 or TGF-β, and the pro-inflammatory IFN-γ, TNF-α or IL-1) and to study the response to endotoxic shock mediated by LPS injection. Targets of our investigation will be:

- Detection of cytokine quantity and quality in plasma;
- Characterization of immune populations through flow cytometry: it will be evaluated the expression of MCH II on professional antigen presenting cells (APC), monocyte and vTcells subsets;
- Evaluation of HDL effect on resident macrophages in terms of cytokine production and mRNA expression.

Interestingly, since Apo AI and S1P are critically involved in macrophage functions, it will be intriguing to characterize macrophage features compared to control ones: resident macrophages from Apo AI KO and S1PR2 KO mice will be polarized in M1 and M2 through the use of specific cytokines from IT-Box-Cy55 (the anti-inflammatory IL-4, IL-10 or TGF-β, and the pro-inflammatory IFN-γ, TNF-α or IL-1), treated with HDL and evaluated cytokine production and mRNA expression. The same study will be performed in bone marrow-derived macrophages, previously treated with M-CSF, or IL-4 from ImmunoTools *IT-Box-Cy55*.

ImmunoTools *IT-Box-Cy55M* for **Fabrizia Bonacina**
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