ImmunoTools IT-Box-139 Award 2012

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Suppression of human T cells by the tumor metabolite 5'-deoxy-5'-methylthioadenosine

The resistance of many malignancies against immunotherapies is often due to tumor-associated immunsuppression. The interaction of tumor cells with circumjacent non-malignant cells creates a suppressive microenvironment. Part of this is an altered metabolism which leads to metabolites like lactate which have been shown to inhibit parts of the immune system. Another metabolite, 5'-deoxy-5'-methylthioadenosine (MTA) is often found accumulated in cancer cells due to a deletion of the catabolizing enzyme Methylthioadenosine-Phosphorylase (MTAP). In vitro experiments showed an inhibition of proliferation and effector function of human $CD8^+$ T cells through addition even of physiological amounts of MTA to the culture. Therefore we are going to examine the influence of MTA on activated and resting human T cell subpopulations like $CD4^+$ (T_H1, T_H2 or T_H17), $CD8^+$ or regulatory $CD4^+CD25^+$ T cells as well as the intracellular mechanism of MTA-mediated T cell suppression.
We have already analyzed the kinetics of the expression of the activating T cell markers CD69 and CD25 in a co-culture of $CD8^+$ T cells with tumor-antigen pulsed dendritic cells with or without supplementation of MTA. Especially the behavior of CD69 gave us an inside into the kinetics of the inhibition via MTA. Hence we would like to analyze further molecules which are associated with the course of T cell activation and memory status: CD27, CD38, CD54, CD62L, CD71 and CD95 as well as CD25 to compare it with our previous data.

Moreover we have seen an impact of MTA on the differentiation and maturation of human Monocyte-derived Dendritic cells. For this purpose we would like to check the co-stimulatory markers CD40, CD80 and CD86.

ImmunoTools IT-Box-139 for Frederik Henrich includes 100 antibodies

FITC - conjugated anti-human CD1a, CD3, CD4, CD5, CD6, CD7, CD8, CD14, CD15, CD16, CD19, CD21, CD25, CD29, CD35, CD36, CD41a, CD42b, CD45, CD45RA, CD45RB, CD45RO, CD49d, CD53, CD57, CD61, CD63, CD80, CD86, HLA-DR, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE - conjugated anti-human CD3, CD4, CD8, CD11b, CD15, CD14, CD18, CD19, CD20, CD21, CD22, CD31, CD33, CD38, CD40, CD45, CD45RB, CD50, CD52, CD56, CD58, CD62p, CD72, CD95, CD105, CD147, CD177, CD235a, HLA-ABC, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE/Dy647 -tandem conjugated anti-human CD3, CD4, CD8, CD14, CD19, CD20, CD25, CD54

APC -conjugated anti-human CD2, CD3, CD4, CD8, CD10, CD11a, CD11c, CD14, CD16, CD27, CD37, CD42b, CD44, CD45, CD59, CD62L, CD69, CD71, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

DETAILS