ImmunoTools IT-Box-Cy55M-Award 2013

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Functional Implications and Interaction of Macrophages in the Tumor Microenvironment of malignant lymphoma

Resistance against chemotherapy is a central problem in the current treatment of B cell malignancies. While many studies have examined the role of cell-intrinsic processes in the context of chemotherapeutic response relatively little is known about the impact of the tumor microenvironment on therapeutic outcome. This microenvironment consists of many different kinds of cells varying between tumors, significantly manipulating malignancy by recruiting or sequestering normal cells to promote their survival, growth or invasion as well as enabling relapses after treatment. Macrophages are present in the microenvironment of most tumors – designated as tumor associated macrophages (TAM) – and are often correlated to a poor prognosis.

Chronic lymphocytic leukemia (CLL) is the most frequent type of leukemia in the western world. Here tumor cells are particularly dependent on signals from the tumor microenvironment for malignant proliferation and survival of chemotoxic therapy.

The focus of the PhD thesis is to define functional characteristics of macrophages in anti-leukemic therapy as there are promising hints that this cell type plays a major role in generating a micro milieu which enables a refractory niche to therapies like the treatment with chemotoxic agents.

Previous experiments could show that in context of certain treatment strategies cytokine induction seems to be a relevant factor in propagating a defined macrophage phenotype displaying effector functions and revoking therapy resistance.

To clarify functional mechanisms behind the crosstalk between macrophages and leukemia cells we would like to use different cytokines like GM-CSF, M-CSF, IL-4, INF-γ to generate different subtypes of macrophages.

Furthermore we are interested in stimulating macrophages with cytokines like VEGF, TNF-α, MIP1-β, IL-1α, IL-1β, IL6, IL-10, IL27 and examine to which extent these stimulation leads to changes in subtype and function of the macrophages to set this in context with observations in related functional experiments *in vivo* and in *vitro*.

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Taken together the ImmunoTools Award would immensely contribute to my work allowing the generation of experiments which enable broader insights into the interaction of tumor associated macrophages and leukemic cells.

By identifying the responsible mechanisms new targets can be determined and used for the development of new therapies.

ImmunoTools *IT-Box-Cy55M* for **Daniela Vorholt**
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

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