ImmunoTools IT-Box-Cy55M-Award 2013

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Interplay between iNKT cells and tumor microenvironment in prostate cancer immunosurveillance

Purpose of this PhD project is to unravel the role of invariant NKT cells in shaping tumor microenvironment. NKT cells are an unique subset of T cells that bridges innate and adaptive immunity. They are characterized by the expression at the same time of NK cells markers, such as NK1.1, and a semi-invariant Va14-Ja18 TCR in mouse, that recognize lipid antigens on the surface of APC cells, presented by the MHC I–like molecule CD1d.

Following TCR triggering, these effector-memory T cells undergo a rapid and potent activation, producing high amounts of Th1 (IFNg, TNFa, IL2, IL7), Th2 (IL4, IL10, IL13) and Th17 cytokine, and upregulating critical factors such as CD40L and FASL.

Their unique ability to exert both pro-inflammatory and regulatory roles makes iNKT cells very attractive, especially in oncology, as they are regarded as key players in cancer immune surveillance. Indeed, iNKT cells enclose the potential for an anti-cancer response, both directly, via killing tumor cells, and indirectly, acting on tumor microenvironment. In particular, as far as microenvironment is concerned, iNKT cells are known to interact with critical cell subsets in tumor microenvironment, such as $CD25^{+}$ $CD4^{+}$ regulatory T cells, Myeloid Derived Suppressor Cells (MDSC) and Tumor Associated Macrophages (TAMs).

At present, an increasing number of reports are trying to elucidate the complex relationship between the presence or the functionality of iNKT cells and human cancers. It is noteworthy that iNKT are found defective in proliferation and in Th1 functionality in many tumors, but it is even more interesting that such defects appear to be reversible (Novak M et al., 2010).

Hence, my goal is to deeply characterize the status of iNKT cells, their relationship with tumor microenvironment and their possible employment or functional modulation to originate and sustain anti-tumor responses.

To do this, I am employing the Transgenic Adenocarcinoma of Mouse Prostate (TRAMP) model, in which we reported that the lack of iNKT cells correlates with an

earlier onset and a faster progression of the disease, independently of CTLs action (Bellone M et al., 2010).

ImmunoTools *IT-box Cy55M* would be of substantial help in studying iNKTs contribution in this disease, in-vitro by using co-coltures approaches, ex-vivo by comparing for instance the cytokine production profile in normal and iNKT KO ($Ja18^{-/-}$) mice under different condition, and potentially in-vivo, using cytokines to drive iNKT cells in creating an anti-tumoral microenvironment.

Reference:
Bellone M, Ceccon M, Grioni M, Jachetti E, Calcinotto A, Napolitano A, Freschi M, Casorati G,Dellabona P. iNKT cells control mouse spontaneous carcinoma independently of tumor-specific cytotoxic T cells. PLoS One. 2010 Jan 13;5(1):e8646

ImmunoTools *IT-Box-Cy55M* for **Filippo Cortesi**
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