ImmunoTools *special* Award 2018

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Myeloid-derived suppressor cells (MDSC) as regulators of T cell responses and contributors of disease progression

Myeloid-derived suppressor cells (MDSC) are the activated stage of immature myeloid cells residing mainly in the bone marrow that upon the influence of factors released under inflammatory conditions like infection and sepsis, acquire suppressive functions. MDSC flow cytometry analyses showed that they express markers like Gr-1 and CD11b commonly expressed by other immune cells and hampering their characterization and distinction from immunogenic cells. Dissecting the Gr-1 epitope into Ly-6C and Ly-6G epitopes with help of these two different antibodies improved their phenotyping. Closely related to monocytes and granulocytes due to their nuclear shape upon histological visualization, they were classified as Monocytic- (Mo-MDSCs) and polymorphonuclear- (PMN-MDSCs) cells. It was established in parallel that both of the subsets were able to suppress T cell responses although by different mechanisms; the former mainly by nitric oxide (NO) and the later by reactive oxygen species (ROS) production.

Originally described in tumor-bearing mice, it was observed that their development and proliferation were dependent on growth factors and cytokines released during this abnormal condition. T cell impairment was dependent on the presence of MDSC and their ablation resulted in tumor size reduction and expansion of host life.

Since several years our work has been dedicated to explore the different aspects of MDSC, mainly their origin, expansion/accumulation and suppressor functions. Last year we published an article where we investigated the effects of different growth factors on MDSC generation and activation. We observed that fresh bone marrow cells cultured for 3 days in the presence of GM-CSF or M-CSF reached a "licensed" stage which was required for activation into a suppressive phenotype (NO production) when stimulated with LPS/IFN-γ or a cytokine cocktail composed by IFN-γ/IL-10/IL-1β/TNF. On the other hand we also observed that not all growth factors could perform such a job since G-CSF or Flt3L failed to generate MDSC.

Our paper's findings led us to ask now for new questions mainly related to the origin of MDSC since their development is tightly linked to growth factors and cytokines.

In the first part of this project we would like to determine which other growth factors and cytokines are involved in MDSC expansion and generation. ImmunoTools products like rm Flt3L/CD135, rm GM-CSF, rm G-CSF, rm IFNγ, rm IL-1αI, rm IL-1β, rm IL-3, rm IL-4, rm IL-6, rm IL-10, rm IL-27, rm IL-33, rm LIF, rm M-CSF, rm TNF and rm VEGF-A (as single factors or in different combinations) would be of great value in order to answer this question. By using the ImmunoTools CD11b APC-conjugated antibody MDSC expansion could be also appreciated.

The second part of the project involves the evaluation of the T cell response when cultured with the *in vitro* generated MDSC. ImmunoTools CD4 and CD8 antibodies, both APC-conjugated plus Annexin V FITC-conjugated and CD247 PE-conjugated would help us in the evaluation of T cell suppression since T cell death or down-regulation of the T cell receptor zeta chain (CD247) are both consequences of T cell impairment through NO by MDSC. Moreover an ImmunoTools ELISA-kit for mouse GM-CSF detection would be of great value for analysing mouse serum samples when the *in vitro* findings will be *in vivo* translated.

ImmunoTools *special* Award for **Eliana Ribechini** includes 25 reagents

FITC - conjugated Annexin, anti-mouse dCD247

APC - conjugated anti-mouse CD4, CD8a, CD11b

recombinant mouse cytokines: rm Flt3L/CD135, rm GM-CSF, rm G-CSF, rm IFNγ, rm IL-1αI, rm IL-1β, rm IL-3, rm IL-4, rm IL-6, rm IL-10, rm IL-27, rm IL-33, rm LIF, rm M-CSF, rm TNF and rm VEGF-A

mouse ELISA set (for one 96 plate): rm GM-CSF

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