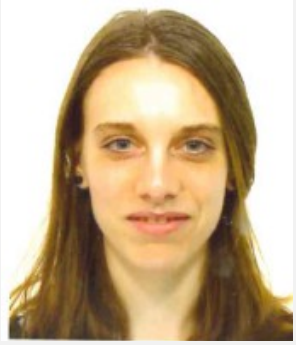
ImmunoTools *special* Award 2019



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Investigation of IgA function in colorectal cancer: shield or weapon?

Background

Colorectal cancer (CRC) is one of the most common malignancies in the world and among the leading causes of tumor-related mortality. Hence the demand for new therapeutic approaches and the necessity to better investigate the promising field of immunotherapy. What happens in the tumor microenvironment (TME) is the principal issue of cancer immunotherapy although this TME-centered view is about to change because of an increasingly growing understanding of the clinical importance of the tumor macroenvironment[1]. The tumor macroenvironment is intended as the systemic tumor environment, comprehensive of all "cancer-promoting networks beyond tumor beds" and the analysis of the tumor/immune system crosstalk at the systemic level could result in new therapeutic options for CRC. In this light, our work describing the changes of the B cell subset following tumor progression in the *Apc*$^{Min/+}$ mouse model of intestinal cancer, gains considerable interest. A peculiar and intriguing involvement of IgA response in the adenomatous transformation was highlighted and requires further exploration[2].

Objectives

The scientific project subject of this "ImmunoTools special Award 2019" proposal comes from the peculiar involvement of the IgA response in the adenomatous transformation. Understanding whether this IgA skewing is peculiar of the *Apc*$^{Min/+}$ mouse, recurrent in other models of CRC, or if it rather represents a sort of wake-

up call for the presence of a developing tumor in general, will be one of the principal objectives. Due to the fundamental role of IgA in protecting mucosal surfaces, little is known on how the systemic IgA system works and how it can be regulated. With a view to CRC care, deciphering the meaning of this IgA skewing and elucidating the mechanisms suited to its modulation might be helpful for the regulation of tumor progression and in providing potential immunotherapy targets.

Methods

Since the IgA story represents the common thread of this project, one of the main tasks is aimed in deepening into the evidences emerged from the study of the *Apc*$^{Min/+}$ mouse and in searching a correlation with other CRC models. In particular, due to the observation that splenic *Apc*$^{Min/+}$ B cells spontaneously release large amounts of IgA and are enriched in IgA-switched cells, activation-induced cytidine deaminase (AID) expression will be analyzed in B cells purified from the spleen of 18-weeks old wild-type and *Apc*$^{Min/+}$ mice. Cytokines known to induce IgA switching will also be analyzed by ELISA among total splenocytes (**ImmunoTools**). B cells isolated from organs other than the spleen (peritoneum, LNs, bone marrow) will be assessed for IgA switching and release, under basal conditions and following activation with specific cytokines and/or immune cell types that interact with B cells and are known to play a role in class switch recombination.

The selected **ImmunoTools** recombinant mouse cytokines will be used to mimic the tumor environment in our *in vitro* experiments while instead the **ImmunoTools** anti-mouse antibodies were chosen on the basis of the cell populations that we aim to follow by flow cytometry.

The dosage of stem cell factor (SCF) by ELISA is instead of interest since a potential role for SCF as a tumor marker of colorectal cancer has been suggested[3].

References

1. Rutkowski MR, Svoronos N, Perales-Puchalt A, Conejo-Garcia JR. The Tumor Macroenvironment: Cancer-Promoting Networks Beyond Tumor Beds. Advances in cancer research 2015; 128:235-62.

2. Mion F, Vetrano S, Tonon S, Valeri V, Piontini A, Burocchi A, et al. Reciprocal influence of B cells and tumor macro and microenvironments in the ApcMin/+ model of colorectal cancer. OncoImmunology 2017; 6: e1336593.

3. Mroczko B, Szmitkowski M, Wereszczyńska-Siemiatkowska U, Okulczyk B. Stem cell factor (SCF) and interleukin 3 (IL-3) in the sera of patients with colorectal cancer. Dig Dis Sci. 2005 Jun;50(6):1019-24.

ImmunoTools *special* AWARD for **Mion Francesca**, includes 25 reagents

FITC - conjugated anti- mouse CD3e, CD19, CD45R, CD54, CD154
PE - conjugated anti- mouse CD3e, CD19, CD45R, CD54
APC- conjugated anti- mouse CD3e, CD49d, CD19

recombinant mouse cytokines: rm IL-6, rm IL-10, rm IL-33, rm MIP3a / CCL20, rm sCD40L / CD154 , rm SCF, rm SDF-1a / CXCL12a, rm SDF-1b / CXCL12b, rm TNFa

mouse ELISA-set SCF

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