ImmunoTools *special* Award 2014

Enrico Catalano, PhD student

Supervisor: Prof.ssa Rimondini

Department of Health Sciences, University of Eastern Piedmont "A. Avogadro", Via Solaroli 17, 28100 Novara, Italy

The role of the immune microenvironment in tumor progression.

From many studies over the past decades, it is clear that the immune system plays a critical role in surveillance against tumor development. Immunodeficient mice defective in interferon (IFN)-γ, perforin, T cell, or NK cell functions develop tumors spontaneously. Multiple lineages of immune cells are involved in antitumor responses. It has long been established that NK cells are able to kill tumor cells in various cancer models. Tumor development and progression are influenced by modifications to tumor parenchymal cells or their microenvironment. One important mechanism of escape from immune surveillance is the selection of poorly immunogenic tumor cells. Alternatively, modification of the microenvironment may also result in the acquisition of a “procancer” profile that encourages tumor outgrowth. These procancer modifications include the expression of antiapoptotic molecules which prevent tumor cell death; growth factors which encourage tumor outgrowth, and immunosuppressive mediators such as VEGF, transforming growth factor-β (TGF-β), interleukin (IL)-10, indoleamine 2,3-dioxygenase (IDO), and programmed cell death-ligand 1 (PD-L1) which suppress antitumor immunity. Toll-like receptor (TLR) pathways such as TLR4 activation on tumor cells have also been shown to directly stimulate tumor growth. Our investigations have underlined the importance of the tumor microenvironment on the clinical evolution of cancer. The molecular and cellular nature of the tumor immune microenvironment influences disease outcome by altering the balance of suppressive versus cytotoxic responses in the vicinity of the tumor. Recent developments in systems biology have improved our understanding of the complex interactions between tumors and their immunological microenvironment in various human cancers. Effective tumor surveillance by the host immune system protects against disease, but chronic inflammation and tumor “immunoediting” have also been implicated in disease development and progression. Accordingly, reactivation and maintenance of appropriate antitumor responses within the tumor microenvironment correlate with a good prognosis in cancer patients. Improved understanding of the factors that shape the tumor microenvironment will be critical for the development of effective future strategies for disease management.

Our studies revealed an association between the expression of intratumoral proinflammatory genes and superior patient survival. We discovered that a 14-gene immunological signature is predictive of patient survival, especially at the early stages of the disease. These 14 immune genes encode chemokines CXCL10, CCL5, and CCL2; cytokines IFNγ, TNF, and IL-6; pattern recognition receptors TLR3 and

TLR4; T cell markers CD8A and TBX21, and NK cell marker NCR3. In my PhD project, I showed that IFN-γ and TLR3 ligand-induced intra-tumor chemokine expression promotes infiltration by cytotoxic T cells and NK cells to enhance tumor cell apoptosis and reduce tumor cell proliferation.

We would like to analyze if other immunological receptors could be included in the interrelations between immune microenvironment and tumor progression. For this purpose we would like to screen the following antibodies of ImmunoTools for these receptors: CD3, CD4, CD7, CD8, CD9, CD10, CD11c, CD14, CD16, CD19, CD21, CD22, CD25, CD27, CD37, CD38, CD40, CD42b, CD44, CD46, CD56, CD59, CD61, CD62L, CD62P and it could be a great opportunity to extend our research.

ImmunoTools *special* AWARD for **Enrico Catalano** includes 25 reagents

FITC - conjugated anti-human CD3, CD4, CD7, CD8, CD9, CD10, CD11c, CD14, CD16, CD19, CD21, CD22, CD25, CD27, CD37, CD38, CD40, CD42b, CD44, CD46, CD56, CD59, CD61, CD62L, CD62P,

DETAILS