ImmunoTools *special* Award 2014

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Role of innate immunity during tumor progression and pregnancy

During the early phases of pregnancy uterus shifts from a controlled neo-inflammatory phase (useful for implantation) to generate an immunologically privileged organ (which maintains tolerance) strictly associated to the placenta. In decidual tissue the presence of cells able to release pro-angiogenic factors involved in building/remodeling of vessel, is fundamental for a successful pregnancy. Decidual NK cells (dNK) represent 50-70% of decidua infiltrating lymphocytes (DILs) and display unique phenotypic and functional properties [1-3]. Thus, they release peculiar cytokines and chemokines (IL-8, VEGF, SDF1a and IP10) involved in neo-angiogenesis, tissue remodeling and placentation. In spite of their high content of cytolytic granules, dNK cells are poorly cytolytic [4]. In addition, upon interaction with $CD14^+$ myeloid cells, they can stimulate regulatory T cell expansion that is involved in feto-maternal tolerance [3]. However, the role of dNK cells, as well as, their interactions with immune cells present in decidual tissues during early pregnancy, remains poorly understood. A better characterization of these cells may offers important clues for a better understanding of major physiological mechanisms occurring in the early phases of pregnancy.

Besides T lymphocytes, also NK cells are thought to play an important role in anti-tumor immunosurveillance. While T cells have been extensively explored, limited information exists on the role of NK cells [5-7]. In particular, the anti-tumor activity of NK cells is based on the capability of recognizing and killing tumor cells, while sparing normal cells. The NK cell function is mediated by an array of activating receptors. These receptors recognize ligands that can be up-regulated by tumor transformation [8-9]. Their activity can be counteracted by inhibitory receptors upon interaction with HLA-class I molecules, expressed by normal cells but down-regulated in tumor cells [8-9]. In clinical studies, high number of tumor infiltrating NK cells has been reported to represent a positive prognostic marker and the low NK-mediated cytolytic activity correlated with an increased risk of cancer. However, in human solid tumors, only few infiltrating NK cells can be detected and the anti-tumor activity of these

cells was inhibited by tumor microenvironment [10]. In particular, we are interested to know the role of NK cells infiltrating tumors and the ability of different cytokines in inducing a potent NK cell-mediated anti-tumor activity. These results may offer various new opportunities to treat primary or metastatic tumors by inducing/potentiating NK cell anti-tumor activity.

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