ImmunoTools *special* Award 2014

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Radiation Oncology: Monitoring irradiation-induced modulation of the immune-inflammatory response in a murine breast tumor model by immunostaining and flow cytometry analysis.

Despite recent improvements in screening and treatment, breast cancer remains the most common cancer type and the second-leading cause of cancer-related death in women worldwide. Survival for women diagnosed with early breast cancer is around 80% at 10 years, however in metastatic disease survival rate remains discouraging, with less then 20% after 5 years. Radiotherapy is a major therapeutic option in breast cancer. While it clearly improves survival, emerging evidence indicates that in relapsing disease radiotherapy may have the opposite effect, namely promote metastasis. Experimental evidence cumulated in the recent years revealed that cancer develops and progress as complex multicellular disease, involving mutual interactions between the cancer cells and the surrounding, non-malignant tissue, the tumor microenvironment (TME). The TME consists of extracellular matrix proteins, fibroblasts, endothelial cells and a variety of infiltrating immune and inflammatory cells**.** It has been shown in a number of tumor models that radiotherapy, similarly to chemotherapy, induces severe TME modifications. Radiation-induced responses typically include vascular damage followed by hypoxia, accompanied by massive mobilization of bone marrow-derived inflammatory cells. Specific subsets of tumor-associated macrophages (TAMs) or their precursors are the predominant cellular components in mouse and human tumors, mostly accumulating in hypoxic regions. TAMs were reported to exert both anti- or pro-tumorigenic activities, which may ultimately play a crucial role in determining anti-cancer therapy efficacy. However, their specific contribute in the context of irradiation has only been marginally investigated. Our laboratory has previously reported that bone marrow-derived $CD11b^{+}cKit^{+}$ cells recruited in experimental breast cancers relapsing after radiotherapy promote lung metastasis. In this project we propose to further characterize the dynamical changes occurring in the tumor microenvironment when irradiation is applied to a mammary carcinoma mouse model under different experimental conditions. In the first place we will monitor acute and chronic effects of local radiotherapy on tumor-infiltrating inflammatory cells. To this end we will identify selected populations of recruited cells by cell surface phenotyping and multicolor flow cytometry analysis. We will focus our attention in particular on TAMs supbpupulations, B cells, T cells, NK and dendritic cell populations. Subsequently we

plan to monitor changes in immune and inflammatory cell populations in peripheral blood and in the lung as a site of (future) metastasis. The below-listed set of anti-mouse antibodies set for flow cytometry provided by ImmunoTools would be perfectly suited for these experiments. Results from these experiments have two relevant, potential translational implications: firstly, the identification of specific blood-circulating cell populations associated with tumor relapse and progression after radiotherapy may lead to the definition of biomarkers of tumor progression, and, secondly, these cell populations (or cell surface proteins) may be investigated as potential therapeutic targets via neutralizing antibodies (i.e. for cell depletion or neutralization of selected receptors). This research project is part of our long-term interest in bridging experimental and clinically-oriented cancer research (translational research) with the purpose to improve anti-cancer therapies. Results obtained in this project are likely to have relevant implications in the management of human breast cancer.

ImmunoTools *special* AWARD for **Chiara Secondini** includes 25 reagents

FITC - conjugated anti-mouse CD3e, CD4, CD8a, CD11b, CD19, CD44, CD45, CD45R, CD62L, Gr-1, NK-cells, isotype control IgG2b,

PE - conjugated anti-mouse CD4, CD8a, CD11b, CD19, CD49d, CD62L, Gr-1, NK-cells, isotype control IgG2b,

APC -conjugated anti-mouse CD3e, CD4, CD11b, CD19, CD45, CD49d, CD62L, Gr-1, NK-cells, isotype control IgG2b,

DETAILS