ImmunoTools *special* Award 2014

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Inflammation and chemokines in colorectal cancer

Colorectal cancer is on second place among cancer-related death causes and a significant health problem worldwide. Although most primary tumors can be resected surgically, colorectal cancer frequently spreads to the liver, what is responsible for the high mortality of the disease. For successful metastasis, cancer cells need to invade surrounding tissues, penetrate microvessels, survive in circulation, disseminate to distant organs, form micrometastases, and expand into macrometastases. To progress through these steps, tumor cells often acquire the capability of survival and invasion by activating metastatic signaling pathways or inactivating metastasis suppressor genes (1). Since high mortality rate in colorectal cancer is tightly associated with formation of distant metastasis, it is necessary to search for new biomarkers associated with metastasis and study the possible mechanisms in the development and progression of this complicated disease.

Recent data have shown that soluble attractant molecules called chemokines support the metastasis of certain cancers to certain organs (2). The chemokines comprise a family of small basic chemotactic proteins whose effects are mediated by binding to G-protein-coupled receptors. They were originally identified by their ability to induce migration of leukocytes. Gradients of chemokines have been proposed to attract tumor cells with matching chemokine receptors to specific sites analogous to the directed homing of leukocytes (3). It is becoming increasingly clear that the chemokine network plays an important role in cancer through its effect on the growth and metastasis of tumor cells as well as in manipulating host-tumor interactions (4). Some of the chemokines are associated with breast cancer metastasis. For example CCL2, produced by stromal breast cancer cells, not only plays an important role in development and progression of breast cancer, but also supports lung metastasis formation of 4T1 cells (5). CCL5/CCR5 on the other hand support invasiveness and metastasis in aggressive basal subtype of breast cancer (6). In colorectal cancer, which is the focus in proposed research project, chemokines and their receptors also affect metastasis and invasiveness. For example, CXCR3 supports lymph node metastasis formation (5), CXCL16 inhibits metastasis formation in the liver (7), whereas CCL25 and its receptor CCR9 inhibit invasiveness and metastasis of

colorectal cancer (8). It has also been shown that inactivation of CCR1 leads to inhibition of liver metastasis formation (9), what can have a potential value in case of studies focused on CCL7, for which CCR1 is a receptor.

As inflammation plays an essential role in cancer and many chemokines control cells of the immune system during immune surveillance, their role may be essential in different stages of tumor progression and especially metastasis.

In this project, the effect of different chemokines and their receptors on tumor growth and metastasis will be analysed in mouse model of colon cancer. Moreover, human colorectal tissue microarrays will be used in order to correlate the expression of chemokines and their receptors with different clinical parameters of the patients.

ImmunoTools antibodies would be very useful for me, as tumor samples from mice as well as patients will be analysed by means of flow cytometry in order to check their content for specific types of inflammatory cells that build the tumor microenvironment and are related to certain chemokines.

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ImmunoTools *special* AWARD for **Ewa Kurzejamska** includes 25 reagents

FITC - conjugated anti-mouse conjugated anti-mouse CD3e, CD4, CD8a, CD11b, CD19, CD25, CD29, CD44, CD45, CD62L, CD90, CD117, CD134, CD247, Gr-1, a/b TCR, g/d TCR, isotype control IgG2b,

APC - conjugated anti-mouse CD3e, CD4, CD8a, CD19, CD45, CD49d, isotype control IgG2b, DETAILS more AWARDS