Conclusion: Our data showed that metastasis to lymph nodes and alcohol consumption are the main factors that affect mortality in HNC patients of Tomsk region.

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T93

Immune system contributes to the efficacy of cancer chemotherapy

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Background: Risk of metastasis formation is provided by both tumor cell biological characteristics and the microenvironment features within the primary tumor along with local and systemic conditions for metastatic niche formation. The inflammatory infiltration has been shown to strongly impact on tumor progression (Whiteside, 2013). Dronca et al. (2011) showed that immunosuppressive factors in the tumor microenvironment may impair not only local immune responses but also disturb systemic immunity. Zitvogel et al. anticipate that the comprehension of the mechanisms governing the immunogenicity of cell death will have a profound impact on the design of anticancer therapies.To study the impact of immune system on clinical response to neoadjuvant chemotherapy and metastasis-free survival in breast cancer patients.
Materials and methods: 350 patients with newly diagnosed invasive breast cancer treated with neoadjuvant chemotherapy (NAC) were enrolled into the study. The procedures were made in accordance with the Helsinki Declaration. Clinical response to chemotherapy, the 5-year metastasis-free survival and all major clinical and morphological parameters were determined. The original method of multidimensional data visualization was applied to present the immune system state as integral entirety in visual image for classification of patients with different risk of metastasis (NovoSpark Corporation, Canada). Copy number aberrations (CNA) of cytokine gene regions in tumor specimens were tested using high-density microarray platform CytoScanTM HD Array (Affymetrix, USA). Cytokine gene polymorphism was analyzed. Subpopulations of lymphocytes and macrophages were determined within the primary tumors by IHC.
Results: We found, that favorable clinical immediate response to preoperative chemotherapy was related to the high levels of IL-1beta, TNF-alpha and IL-10 production by peripheral mononuclear cells before the treatment. This correlation was further confirmed by data from the study on association between cytokine gene functional polymorphism and response to NAC. We used NovoSpark Corporation visualization approach allowing the representation the immune system state as integral unit and to discriminate breast cancer patients with high and low risk of haematogeneic metastasis. When estimated before cancer treatment, 95% of breast cancer patients had risk of metastasis. The neoadjuvant chemotherapy and surgical tumor removal reduced the risk of tumor progression to 62–71%. However, in a year after adjuvant chemo- and radiotherapy, the patient group with high risk of metastases increased to 81% again. Thus, the cancer treatment can change the primarily estimated outcome prognosis in breast cancer patients, and the monitoring of immune system is a promising approach to predict the risk of cancer progression or resistance to the therapy. We have found the connection between the profile of intra-tumor inflammatory elements and chemotherapy efficacy.Cytokine gene expression may be influenced by the chromosome anomalies (CNA – Copy Number Aberration) – deletion and amplification – of cytokine gene loci in tumor cells. We found the close relation between the clinical response to NAC and gain of function of IL-10 and CHI3L1 (YKL40) genes. In contrast, loss of TNF-alpha and IL-17 gene function due to corresponding CNA was associated with good response to NAC. Metastasis-free survival of breast cancer patients was shown to be closely related to CNA.
Conclusion: The parameters of the activation of systemic and intra-tumoral immune system by growing tumor and its dissemination have to be validated in order to identify the new prognostic markers for the efficiency of the neoadjuvant chemotherapy.

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P133

DNA inhibits dsRNA-activated NF-kB-based inflammation in tumour cells: The role of Ku protein

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The strong connection between cancer-related inflammation and tumour development with pattern – recognizing receptors (PRRs) activation results in identification of new target molecules that could lead to improved cancer diagnosis and treatment. TLR3, RIG1 and MDA5 synthetic ligand poly(I:C) was shown to trigger apoptosis in cancer cells. However, TLR3 signaling also includes NF-kB transcription factor which has emerged as endogenous tumour promoter via stimulation of pro-inflammatory tumour microenvironment, enhancement of angiogenesis, tumour cell proliferation and metastasis. Thus down regulation of NF-kB-mediated effects after TLR3 activation is needed for implementation of TLR3 ligand-based therapy into clinical trials.

We have earlier demonstrated that DNA and sequence specific ODNs inhibit poly(I:C)-induced production of pro-inflammatory cytokines in human primary fibroblasts and endothelial cells (Cherepanova et al., Immunobiology, 2013). Using these specific ODNs and affinity modification/isolation approach combined with subsequent MALDI-TOF the main cellular targets for these ODNs were identified as Ku protein – heterodimer of KU70 and KU80 (Cherepanova et al., Exp. Opin. Biol. Ther., 2012).

The goals of this study are to reveal whether the ODNs target poly(I:C)-induced activation in tumour cells: cervical carcinoma (Hela) and epidermoid carcinoma (A431) and to confirm Ku