Abstract

Colorectal cancer is one of the most common type of malignity. Despite of the existence of numerous studies focused on this carcinoma, there are still many unknown features regarding its diagnosis, treatment or prognosis. In the thesis we focused on the identification of novel prognostics markers that could be useful for the stratification of patients based on the disease outcomes.

In the first study we immunohistochemically assessed expression of two proteins associated with cancer stem cells in the samples of primary colorectal cancer and matched liver metastasis. Goal of the study was to evaluate relation among expression of CD44 and CD133 and overall survival and disease free interval in our set of patients. We observed that increased ratio of CD133 positive compared to CD133 negative tumor glands resulted in longer disease free interval, finding which is opposite to the general view on the CD133 role in the cancer development. Our hypothesis is that we analyzed confined group of patients and followed a bit different goal, where we measured ratio between positive and negative glands in the view-field and not the intensity of staining as the previous studies did.

Our second study was focused on the transcriptional analysis of the selected set of twelve genes using frozen samples from colorectal cancer patients. Main goal was to detect differentially expressed genes between healthy and tumor tissue and relate experimental data to overall survival and disease free interval. In this study we analyzed samples from 53 patients and identified ten genes with altered expression. For portion of analysis we divided patients into two groups based on presence or absence of distant metastasis at the time of primary surgery. Statistically significant associations between gene expression level and clinical data were found. Higher level of *VSNL1* in tumor tissue correlated with longer overall survival. In the group without metastasis we found relation between higher level of *SLC26A2* and longer overall survival, longer disease free survival was related to lower level of *VSNL1* expression in healthy tissue and higher level of *SLC26A2* in tumor tissue. Expression change between healthy and tumor tissue showed that downregulation of *CLDN23* in tumor tissue correlated with shorter overall

survival in the complete group of patients, in the group without distant metastasis we found that downregulation of *SLC26A2* and *ACSL5* and upregulation of *LGR5* related to longer disease free interval.

Our data points out the need to study even markers, whose role in the tumor development seems clear at this moment. To understand our results regarding CD133 protein and *LGR5* mRNA it is necessary to learn more about function of these proteins in biology and pathology of the cell. In the transcription study we showed new markers with the potential to specify prognosis in colorectal cancer patients. These markers could help with the selection of patients for the oncology treatment and could give us indirect insights regarding the tumor biology.