

ABSTRACT

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Colorectal cancer (CRC) is one of the most common cancers in the world and also in the Czech Republic. There are many reasons for such a high prevalence and mortality. In general, we can say, that the level of awareness of risk factors and primary prevention is very low. For example, the inoperability of the tumor, caused by the diagnosis of CRC at a late stage, makes therapy of patients difficult and reduces survival. 5 – Fluorouracil and leucovorin are the gold standard in the treatment of CRC. The targeted therapy has a great success in the palliative therapy and prolongs survival. However, many patients do not respond to adjuvant and palliative therapy well. This failure is often caused by drug resistance. Efflux of cytotoxic drugs out of cells caused by transport proteins of cancer cells. ABC transporters remain among the many elements of drug resistance. Deregulation of gene expression of ABC transporters in tumor cells was discovered in connection with other types of cancer. The aim of this study is to find prognostic markers for CRC and enable improvement of the therapy of patients with CRC. By help of qPCR and statistical analyses statistically significant changes in gene expression were identified that might influence the therapy and prognosis of CRC. Expression of the majority of investigated genes was decreased or unchanged in tumors compared with the non – cancer tissues. Significantly increased expression of ABCB2, ABCC1, ABCC2 and ABCC10 genes in tumor tissue compared to non – cancer tissue was found. After comparing the gene expression of ABC transporters in tumors with clinical data of patients, significant correlations of expression of ABCA7, ABCC6, ABCE1, ABCF1, ABCG2, ABCG8 genes with age was revealed. The expression of ABCB2 gene was significantly higher in tumors of the colon compared with those in rectum. Patients with increased ABCD4 expression in their tumors exhibited shorter disease free survival than patients with lower levels of expression. This study shows ABCD4 is the most interesting candidate, prognostic marker for patients with localized stage of CRC. Subsequent studies will be oriented on functional analysis of this marker.