Abstract

Colorectal carcinoma (CRC) is one of the most common malignancies worldwide with persistently high mortality. As a consequence, high demands are placed on research into this disease. The aim of this study was to evaluate the epidemiology of colorectal carcinoma in the Czech Republic in comparison with worldwide data. We focused on the evaluation of the latest findings in screening and diagnosis, investigated prognostic factors, and also focused on the therapeutic options of CRC. Furthermore, mucin-producing carcinomas are described in detail and mucin itself was confirmed as a risk factor for the prognosis of CRC patients.

The experimental part of the study focused on gene mucin *MUC13* and the *MUC13* - miR-4647 axis, which is associated with adverse prognosis in CRC patients. Samples of CRC and samples of adjacent non-malignant mucosa tissue were used. The samples were collected from patients who underwent surgery at the General University Hospital in Prague, at the Thomayer University Hospital in Prague and at the University Hospital in Pilsen (Czech Republic). The collection of samples took place between 2011 and 2015. The total of 187 samples were collected from patients with sporadic colorectal cancer. The subjects of the study all provided information on their lifestyle habits, body mass index (BMI), diabetes, and family or personal history of cancer.

CRC patients with higher levels of gene *MUC13* expression in tumor tissue showed a worse prognosis and shorter survival compared to patients with lower levels of expression (Gupta, 2012, Chauhan, 2009 a 2012, Shimamura, 2005, Walsh, 2007). In a cell line experiment, we determined that *MUC13* expression levels decreased after ectopic overexpression of miR-4647 by RT-qPCR. In the present study mucinous tumors expressed MUC13 at a lower level compared to adenocarcinomas (25 % vs. 34 %).

In vitro, we confirmed that higher levels of *MUC13* expression were associated with longer survival and higher migration ability of the cancer cells, and conversely, colorectal cancer cells with increased miR-4647 expression formed significantly fewer colonies and exhibited decreased migration ability. These observations confirmed that the decreased survival of CRC patients may be associated with the gene *MUC13* and with decreased miR-4647 expression. Interestingly, also higher expression levels of miR-4647 were associated with shorter patient survival, which is in contrast to our observations of a negative correlation between miR4647 and *MUC13* levels. Clearly the effect on prognosis is of a more complex nature, where other factors may play a role. Further research should clarify the relationship between *MUC13* expression, tumor stage, and prognosis of the malignant process.

MUC13 released from the surface of tumor cells and its serum levels in patients with gastrointestinal carcinomas may be an important diagnostic tool. Given these results, the *MUC13* - miR-4647 axis in colorectal cancer seems very promising with regards to novel therapeutic approaches. We believe that gene *MUC13* might have a significant potential for screening, diagnosis, and treatment of cancer.