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Genes of the microRNA biogenesis pathway are deregulated in Colorectal cancer

Ondrej Slaby, Petra Faltejskova, Marek Svoboda and Rostislav Vyzula
Masaryk Memorial Cancer Institute, Czech Republic

MicroRNAs (miRNAs) are small non-coding RNAs 18-25 nucleotides long that regulate gene expression on post-transcriptional level. Therefore, their production and maturation have to be strictly regulated. Their biogenesis starts with the transcription, which is followed by several steps that lead to processing of primary transcripts to mature miRNAs. Each step of this pathway is sophistically regulated and any disruption of control mechanisms may leads to the cancer occurrence. The aim of this study was to analysethe expression of the crucial genes involved in the biogenesisof miRNAs in colorectal cancer (CRC).

Expression of 19 selected genes (EIF2C1-4, GEMIN4, DDX20, TARBP2, DICER1, XPO5, DROSHA, DGCR8, POLR2A, DDX5, DDX17, ADAR, ADARB1, TNRC6A, LIN28A/B) has been analysed in tumour tissues of 120 clinically characterized patients with CRC and in 120 parallel healthy tissues byqRT-PCR. Using Wilcoxon test, genes with different expression between tumour tissue and healthy tissue have been identified. Subsequently, Kruskal-Wallis test has been used to find any correlation with the clinical-pathological features of the patients.

We have found significantly higher expression of POLRIIA, ADAR, ADARB1, DGCR8, DDX5, DDX17, DROSHA, XPO5, EIF2C1-C4, TARBP2, TNRC6A, GEMIN3, DDX20 and DICER1 ($P < 0.0001$) and significantly lower expression of LIN28A in tumour tissue of CRC patients. Moreover, negative correlation between the expression of AGO3 and clinical stage of patients ($P = 0.0017$) and grade ($P = 0.0151$) and positive correlation between the expression of DICER1 ($P = 0.0230$) and DROSHA ($P = 0.0212$) and grade of patients has been observed.

Our results show that changes in the expression of genes associated with biogenesis of miRNAs may be associated not only with the origin, but also to progression of CRC and therefore, these molecules could serve as potential new biomarkers or therapeutic targets.This work was supported by Grant IGA NT/13860-4/2012 and NT13549-4/2012 of the Czech Ministry of Health.

on.slaby@gmail.com