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Oncogenomic investigation in the field of colon cancer carcinogenesis

Peter Pocza
Budapest, Hungary

In the past decades, colorectal cancer became one of the main foci of cancer research. One of the reasons of this is that colorectal cancer is one of the most serious problems of the public health. On the other hand, the relative ease with which pathological specimens can be obtained by either surgery or endoscopy from different stages of tumor progression has facilitated the application of genomic technologies.

In our study, we have investigated the gene expression profiles of lymph-node metastasis negative and distant metastasis positive colon cancer tissues compared to the adjacent non-cancerous mucosa from surgical resections, in order to improve our understanding of the genetic mechanism of carcinogenesis in human colorectal cancer and to identify new potential tumor markers useful for clinical practice. Two-colour whole human genome oligonucleotide microarray was carried out and significantly deregulated genes were analyzed. Our results were validated on extended pieces of specimens of human colorectal cancer and on colon cancer cell lines. In the course of pathway analysis we found that the decreased level of IGF-1 was associated with the decreased level of MDR1/P-gp and regulated via the MAPK-cascade. After the validation on tissue samples we provided evidence that increased IGF-1 resulted in the increased expression of MDR1/P-gp via the MAPK signaling pathway in three human colon cancer cell lines.

Our data gives new insights into the genetic mechanisms underlying neoplastic transformation of colorectal.