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Sporadic colorectal cancer: From genetic make-up to complex phenotypic measurement, from risk determination to prognostic markers

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Colorectal carcinogenesis (CRC), as a complex process, involves a plethora of events resulting in both genomic and chromosomal instabilities. The theories underlying carcinogenic process point out either the role of somatic mutation or the surrounding microenvironment. However, neither of them explains all features of cancer. Uncontrolled proliferation and genomic instability point to the DNA repair and DNA damage response are the key players. In the present study, we will overview several biomarkers in mapping heterogenous complex CRC disease and providing prognostic information. Variants in genes involved in several important pathways, such as DNA repair, cell cycle control, folate metabolism and methylation, insulin resistance and obesity, ABC transporters, selenoprotein genes, genes involved in inflammatory/immune response have shown various degree of association with CRC risk. We also present the data on mutations in high risk genes involved in colorectal carcinogenesis. Gene expression levels were determined in relevant pathways and complemented with other important parameters, such as epigenetic regulators of transcription by methylation. Additionally, the role of post-transcriptional regulation via miRNA or lncRNA was investigated in relation to the risk of CRC and the efficacy of chemotherapy. We have discovered several genetic and epigenetic markers affecting independently the prognosis of CRC. Functional DNA repair tests (complex phenotype) have been implemented as markers of individual susceptibility to sporadic CRC and its prognosis.

An application of the whole set of various biomarkers, covering genetic, epigenetic and functional aspects is inevitable to define the phenotypic landscape of the disease and to delineate the individual response to the therapy.

Biography

P Vodicka graduated at the Medical Faculty, Charles University, Prague and in 1986 obtained PhD in Biochemistry. He worked as Postdoctoral Fellow at the Finnish Institute of Occupational Health, Helsinki, Finland (1987-1990) and as Visiting Scientist at Karolinska Institute, Huddinge, Sweden (1990-1993). Since 2002 he heads the Department of Molecular Biology Cancer, Institute of Experimental Medicine, Academy of Sciences of Czech Republic, Prague, Czech Republic. He has published more than 150 (more than 3000 citations a HI 32) articles. Since 2004, his main research topics are focused on the DNA and chromosomal damage and DNA repair functional tests in humans and on transient biomarkers in the onset of gastrointestinal cancers. In 2012 he edited the special issue in Mutagenesis, *Colorectal Cancer-Current Insights into Susceptibility*.

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