P. Vodicka et al., J Mol Biomark Diagn 2014, 5:2
http://dx.doi.org/10.4172/2155-9929.S1.021

OMICS Group Conferences
Accelerating Scientific Discovery

5th International Conference on
Biomarkers & Clinical Research
April 15-17, 2014 St. Hilda's College - University of Oxford, UK

The use of biomarkers to characterize colorectal cancer: From genetic make-up to complex phenotypic measurement

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Majority of cancer cases occurs sporadically as a consequence of complex interplay between genetic variants and environmental factors. Colorectal carcinogenesis (CRC) involves a plethora of events, such as uncontrolled proliferation and genomic instability, which point to the DNA repair and DNA damage response as to the key players. Here we overview several biomarkers in mapping heterogenous complex disease, which poses a serious health problem worldwide, and provide an excursion into the DNA repair phenotypic reflection in control individuals and CRC patients.

Gene variants involved in pathways, such as DNA repair, cell cycle control, folate metabolism and methylation, insulin resistance and obesity, ABC transporters, seleno proteins, inflammatory/immune response have shown various degree of association with CRC risk. Gene expression levels in relevant pathways were complemented with transcription regulations by methylation. Post-transcriptional regulation via miRNA or lncRNA was evaluated in relation to the CRC risk and the efficacy of chemotherapy. SNPs in miRNA binding sites of *SMUG1* gene affect significantly survival in 5-fluorouracil-treated CRC patients, suggesting the importance of SNPs within miRNA-dependent regulatory regions. Expressions of the specific proteins (mismatch repair, base excision repair) were also assayed for. Functional DNA repair tests have been implemented as biomarkers of the complex phenotype.

Multiple biomarkers, covering genetic, epigenetic and functional aspects, may define the phenotypic landscape of the disease and delineate the individual response to the therapy. Functional DNA repair assays reflect the capacity of the organism to cope with a chronic exposure to numerous environmental and dietary genotoxicants and may also be used as predictive markers in cancer therapy.

Biography

Pavel Vodicka graduated at the Medical Faculty, Charles University, Prague and in 1986 obtained Ph.D. in biochemistry. He worked as postdoctoral fellow at the Finnish Inst. Occupat. Health, Helsinki, Finland (1987-1990) and as visiting scientist at Karolinska Institute, Huddinge, Sweden (1990-1993). Since 2002 he heads the Dept. Molec. Biol. Cancer, Inst. Exper. Medicine, Acad. Sci., Prague, Czech Republic. Pavel Vodicka has published more than 130 (total IF 552.4, 2650 citations a HI 31) 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 (http://mutage.oxfordjournals.org/content/27/2.toc), entitled *Colorectal Cancer-Current Insights into Susceptibility.*

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