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**Epigenome analysis of colorectal cancer: A genome wide approach**

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**ABSTRACT**

Cancer is a global health burden with over 14.1 million new cases annually and projected to increase in the next decade. Colorectal cancer (CRC) contributes around 1.36 million of the total cases worldwide. In Malaysia, the incidence rate of CRC is 21.3 cases per 100,000 population. Many molecular pathways are involved in carcinogenesis including DNA methylation. DNA methylation is important in gene modification and transcription. Genes with high levels of 5-methylcytosine (hypermethylation) in the promoter regions are associated with gene silencing and may alter the signalling pathway that contribute to CRC tumorigenesis. On the other hand, genes with low levels of 5-methylcytosine (hypomethylation) have also been implicated in CRC progression through tumor-suppressor genes or act as oncogenes. Many studies have also revealed the involvement of enhancer regions in regulation of gene expression, hence the demand for a more comprehensive tool for methylation profiling. The aim of this study is to comprehensively characterize the differentially methylated regions involved in CRC pathogenesis. Genomic DNA was extracted from 8 paired matched samples (> 80 % tumor cells) collected from UKM Medical Centre (UKMMC). Bisulfite conversion was performed and the bisulfite converted DNA was subjected to microarray using Human Infinium Epic Beadchip Array. Based on Partek Genomic Suite 6.6 analysis, 25377 genes were significantly differentially methylated on CpG loci (p≤ 0.05), with 10573 hypermethylated and 14804 hypomethylated genes. Pathway enrichment analysis using David Bioinformatics Resources 6.8 revealed involvement of 743 genes in the colorectal cancer pathway, 451 genes in MAPK signalling and 208 genes in Wnt signalling pathway. By overlapping these three different pathways, 30 hyper- and hypomethylated genes were identified. MAPK9, RAC1 and PRKACA are top three hypermethylated genes whereas MYC, PRKACB and PRKCG are the top three hypomethylated genes. This is the first look at the methylation profile of local CRC patients using the latest platform assay. The new knowledge from this study can be utilized for personalized health diagnostics, disease prediction, and monitoring of treatment.