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**Circulating microRNAs as pre-symptomatic predictive biomarkers of colorectal cancer**

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**ABSTRACT**

Colorectal cancer (CRC) is the third most frequent cancer worldwide and the second leading cancer in Malaysia. CRC is mostly asymptomatic until it progresses to the advanced stage. Early detection biomarkers are needed to detect CRC at an early stage to improve survival. Circulating microRNAs have been proposed as biomarkers for the screening of different type of cancers. microRNAs play a significant role in carcinogenesis and have been observed to be dysregulated in many cancers including CRC, and they are also more stable than other nucleic acids even in the circulation. The aim of this study was to discover microRNA(s) which could serve as biomarkers of cancer predisposition as well as for early detection of CRC which will benefit at-risk individuals. We used 50 uL of serum from 5 individuals, taken at the pre-symptomatic stage at recruitment into The Malaysian Cohort project, who had eventually died due to colorectal cancer. These individuals had given written informed consent for future research on their biospecimens. Sera from 5 individuals who did not develop any cancer after five years were used as controls. MicroRNA was purified using column purification technique and converted into cDNA by reverse transcription. The cDNA was then used for SYBR Green-based real-time PCR to quantify and profile expression of the 84 most important microRNAs associated with human serum and plasma. The fold change was analysed using 2-ΔΔCt method and T test was utilized to determine the significance differences between two groups. Using ± 1.5-fold as a cutoff for expression regulation, 13 microRNAs exhibited differential expression. Upon applying a p-value of <0.05, the significant downregulation of hsa-miR-17-3p expression (-2.9644 fold) was identified with a p value of 0.0395. Downregulation of hsa-miR-17-3p could be the potential biomarker for pre-symptomatic of CRC.