Examining Plasma microRNA Markers for Colorectal Cancer at Different Stages

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BACKGROUND: Circulating microRNAs (miRNAs) have emerged as promising biomarkers; however, few miRNAs have been clinically validated in prelude to establishing clinical utility.

HYPOTHESIS: Our large-scale study at different stages of colorectal cancer (CRC) will contribute to identify candidate biomarkers for CRC detection, stage, and prognosis.

METHODS: We screened the levels of 754 miRNAs in 50 individual plasma samples from 10 demographically matched healthy controls and 40 CRC patients (10 each of stage I-IV). Multiple pairwise comparisons among controls and CRC stages revealed candidate miRNAs that were evaluated in 187 CRC cases and 47 healthy controls. Comprehensive analyses identified panels of miRNAs associated with CRC characteristics.

RESULTS: The discovery step identified 22 miRNAs associated with the presence of and stages of CRC. In an independent validation cohort, plasma miR-96 could distinguish stage I-IV CRC patients from controls with an area under curve (AUC) of 0.740; miR-203 could separate stage III-IV CRC patients from stage I-II with an AUC of 0.757; and miR-141 could differentiate stage IV CRC from stage I-III patients with an AUC of 0.851. Survival analyses showed that miR-96 and miR-200b levels were independent prognostic factors for overall survival, and miR-96 levels were significantly associated with overall survival in stage II and III CRC patients. Most of the identified miRNAs were novel as compared to previous studies.