Novel Nucleosomics Serum Biomarkers for the Detection of Colorectal Cancer

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Summary

BACKGROUND: As colorectal cancers are often detected at late tumor stages when prognosis of the patients is poor, powerful blood-based biomarkers are needed for earlier detection. In recent years it has become clear that epigenetic changes to chromatin and its constituent nucleosomes are associated with carcinogenesis and elevated levels of nucleosomes are present in the blood of cancer patients.

We now report a study of the prevalence of genome wide epigenetic signals present in circulating cell-free nucleosomes as potential serum biomarkers for colorectal cancers.

PATIENTS AND METHODS: Serum samples from 90 patients (24 colorectal cancer (CRC), 10 benign colorectal diseases (BCD) and 56 healthy controls (HC)) were tested for the differential diagnostic performance of a novel nucleosomics biomarker 5-methylcytosine modified DNA (NuQ-X). Methodical features including intra- and interassay imprecision were tested using serum pools. To minimize interassay variability, values were transformed to adjusted optical densities and robust statistics were applied for clinical evaluation. Findings were later reevaluated on a set of 113 patients (49 CRC, 26 BCD and 38 HC).

RESULTS: Intra- and interassay reproducibility were 3.4% and 15.3%, respectively. Levels of NuQ-X were significantly decreased in CRC and BCD when compared with HC (p<0.05), although there was no difference between BCD and CRC. For discrimination of CRC from HC, sensitivities were 33% at 95% specificity and 75% at 70% specificity, respectively. The findings were generally confirmed when validated at the second set of patients.

CONCLUSION: Reduced methylation of DNA on circulating nucleosomes detected by the NuQ-X assay can potentially serve as diagnostic tool in CRC patients.















