CANCER SPECIFIC PROFILES OF EPIGENETICALLY ALTERED CIRCULATING NUCLEOSOMES MEASURED BY SIMPLE ELISA DETECT AND DIFFERENTATE COLORECTAL AND PROSTATE CANCER

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SUMMARY

BACKGROUND: Genome wide epigenetic signals are altered in cancer cells. In addition, circulating nucleosome bound DNA fragments contain the same mutations as cancer tissue samples taken from the same subjects suggesting a tumour origin for at least some circulating nucleosomes.
We have developed ELISA tests for circulating nucleosomes (NuQ®) that contain specific epigenetic signals and used these to investigate global epigenetic profiles in the serum and plasma of colorectal (CRC) and prostate (PCA) cancer patients.

METHODS: Serum and plasma samples taken from 39 subjects referred for colonoscopy, 9 male subjects newly diagnosed with PCA and 10 male control subjects were assayed for total nucleosomes as well as nucleosomes containing methylated DNA, and a variety of histone structures including H3K9(Me)$_3$ and MH2A1.1, using NuQ® ELISA kits.

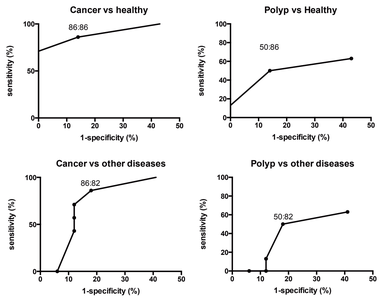
RESULTS: A reduced level of circulating nucleosomes containing methylated DNA was observed in both cancers. The results of two NuQ® assays for circulating nucleosomes containing methylated DNA or MH2A1.1, expressed as a ratio, detected more than 85% of colorectal cancer cases with greater than 85% specificity, both over healthy subjects and over subjects with other (non-cancer) colon diseases, and also detected 50% of precancerous polyps. Similar NuQ® tests for circulating nucleosomes containing methylated DNA or histone modifications were able to detect approximately 80% of prostate cancer cases with 70% specificity. Moreover, as well as being distinct from the profile of healthy subjects, the profiles of epigenetically altered circulating nucleosomes in the two cancers were also different from each other. For example levels of circulating nucleosomes containing H3K9(Me)$_3$ were elevated in CRC but supressed in PCA.

CONCLUSIONS: Serum and plasma profiles of epigenetically altered circulating nucleosomes measured by simple ELISA can detect both CRC and PCA, and differentiate between the two.

RESULTS CRC

Ratio of plasma cell-free nucleosomes containing MH2A1.1, 5-methyl-DNA

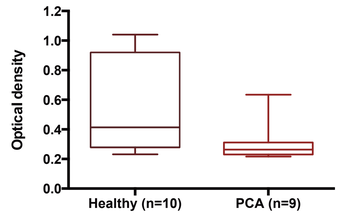
ROC curves



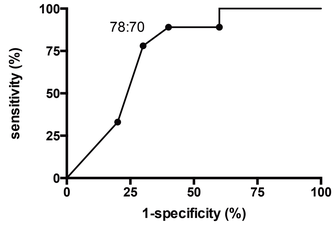
RESULTS PCA

Serum nucleosomes containing 5-methyl-DNA

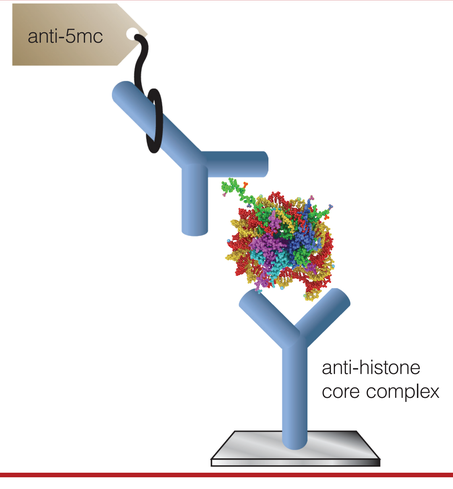
Box plot



ROC curve



EXAMPLE VOLITIONRX NUQ® ELISA



SERUM NUCLEOSOME H3K9(Me)$_3$ IN CRC & PCA