

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

Herzog M, Chapelier M, Cuvelier S, Scoubeau K, Josseaux E, Eccleston M, Micallef J
 Belgian Volition SA, Rue du Seminaire 20A, BE-5000 Belgium. Correspondence: j.micallef@volitionrx.com, +32 81 72 56 46

SUMMARY

BACKGROUND: Immunohistochemistry and other studies show genome wide histone modification, histone variant and DNA modification patterns are altered in cancer tissue. In addition, circulating cell-free nucleosome bound DNA fragments contain the same mutations as cancer tissue samples taken from the same patients suggesting a tumor chromatin origin for at least some circulating nucleosomes.

We have developed serum and plasma ELISA tests for circulating nucleosomes (NuQ®) that contain specific epigenetic signals and used these to investigate global epigenetic profiles in colorectal (CRC) and prostate (PCA) cancer patients.

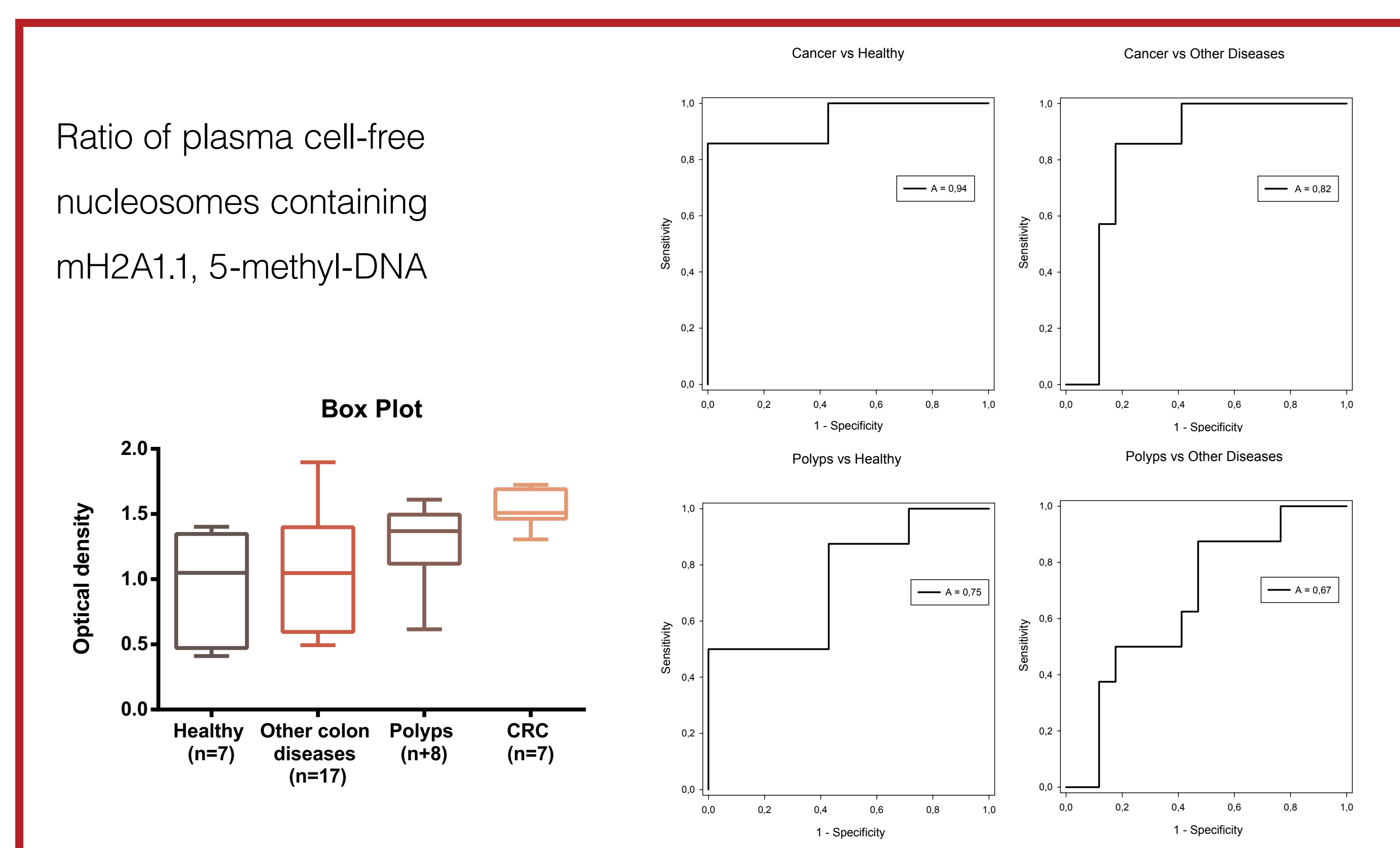
METHODS: Serum and plasma samples taken from 39 subjects referred for colonoscopy, 9 male subjects newly diagnosed with PCA and 10 male control subjects were assayed for total nucleosomes as well as nucleosomes containing methylated DNA, and a variety of histone modifications including H3K9(Me)₃ and H3K4(Me)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, compared to healthy subjects and to subjects with other (non-cancer) colon diseases; 50% of the precancerous polyps were detected as well. Similar NuQ® tests for circulating nucleosomes containing methylated DNA or histone modifications were able to detect approximately 70% of prostate cancer cases with up to 90% specificity.

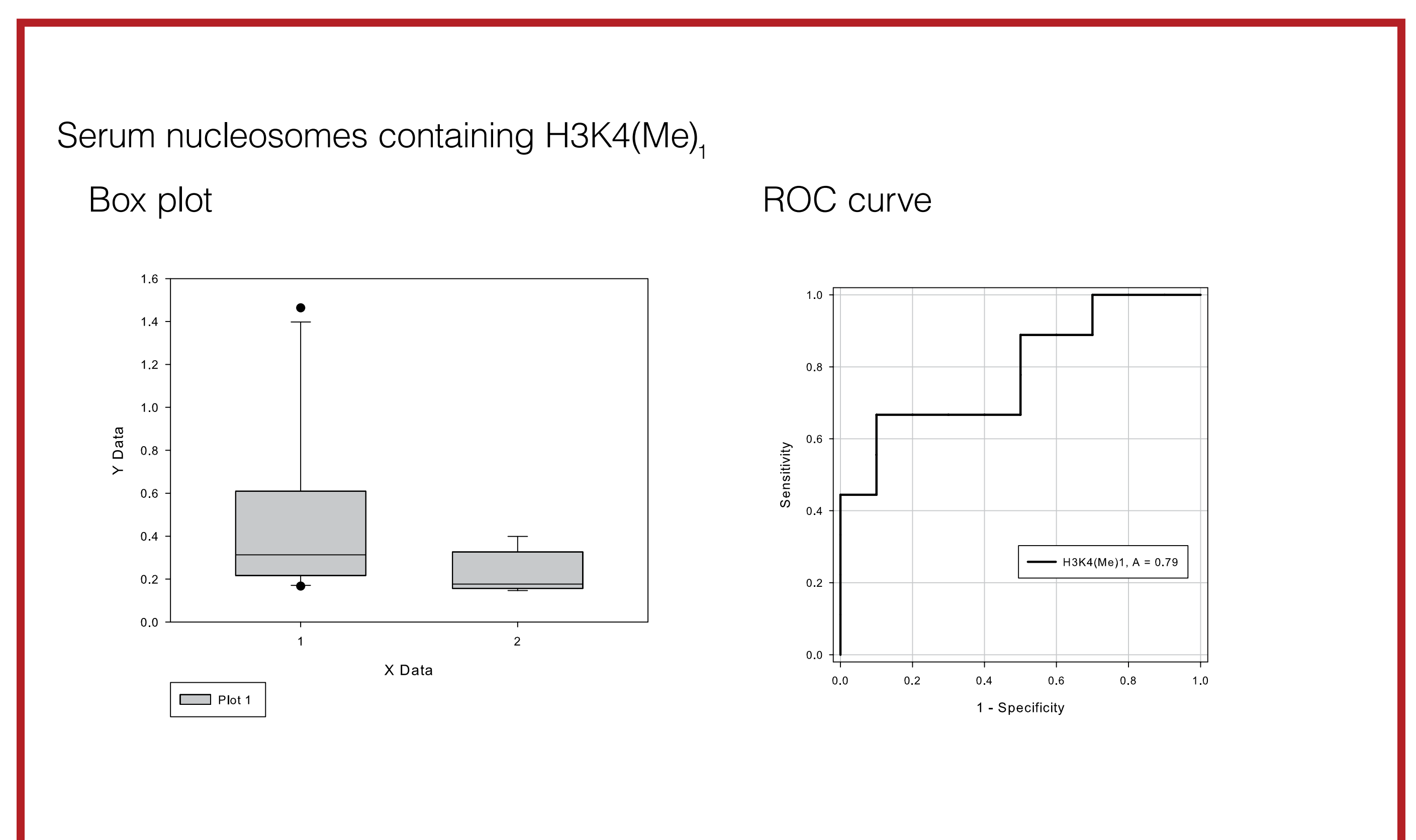
Moreover, as well as being distinct from the profile of healthy subjects, the profiles of epigenetically altered circulating nucleosomes in the two cancers were also different from each other. For example levels of circulating nucleosomes containing H3K9(Me)₃ were elevated in CRC but suppressed in PCA.

CONCLUSIONS: Serum and plasma profiles of epigenetically altered circulating nucleosomes measured by ELISA can detect both CRC and PCA, and differentiate between the two. A larger CRC study involving 4800 subjects referred for colonoscopy is now underway.

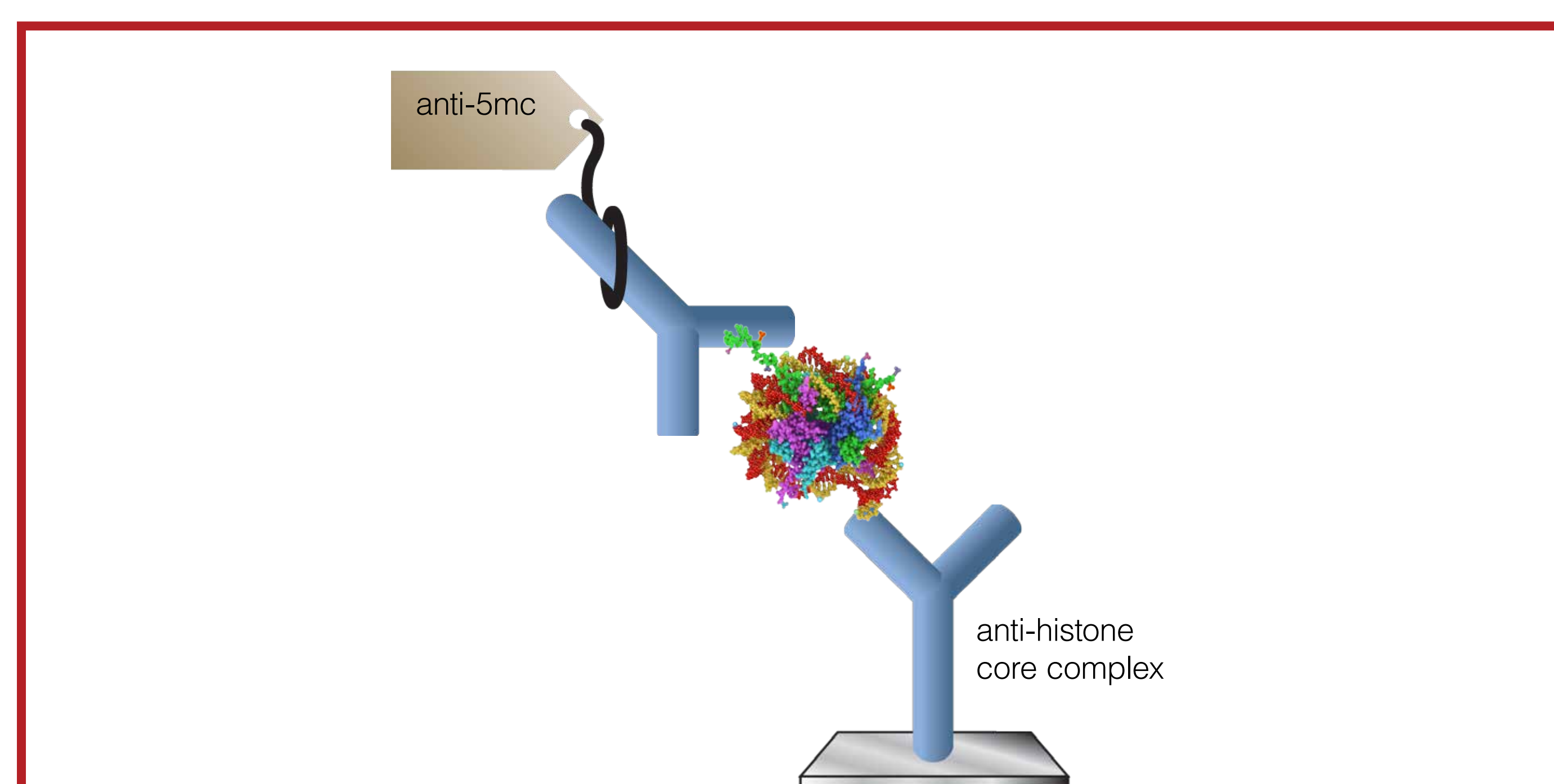
RESULTS CRC



RESULTS PCA



EXAMPLE VOLITIONRX NUQ® ELISA



SERUM NUCLEOSOME H3K9(Me)₃ IN CRC & PCA

