POSTER 4476

EPIGENETICALLY ALTERED CIRCULATING NUCLEOSOMES AS BLOOD BIOMARKERS FOR EARLY DETECTION OF CANCER: CLINICAL STUDIES IN NSCLC, CRC, PCA AND PC

Herzog M[1], Pamart D[1], Cuvelier B[1], Scoubeau K[1], Josseaux E[1], Eccleston M[1], Michael A[2], Pandha H[2], Micallef J[1].

[1]Belgian Volition SA, Rue du Séminaire 20A, B-5000 Namur, Belgium

[2]The University of Surrey, Surrey, GU2 7XH, United Kingdom

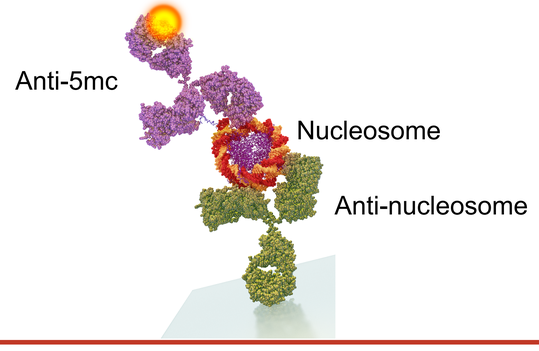
METHODS

BACKGROUND: Chromosome epigenetic structure in cancer is altered with respect to histone modifications, histone isoforms, DNA modifications and in non-histone nuclear protein composition – e.g. the estrogen receptor (ER) in breast cancer. Short (<180bp) fragments of tumor-derived cfdna circulate in the blood of cancer patients as mono-nucleosomes.

AIM: To evaluate epigenetically altered nucleosomes as blood biomarkers for early cancer detection

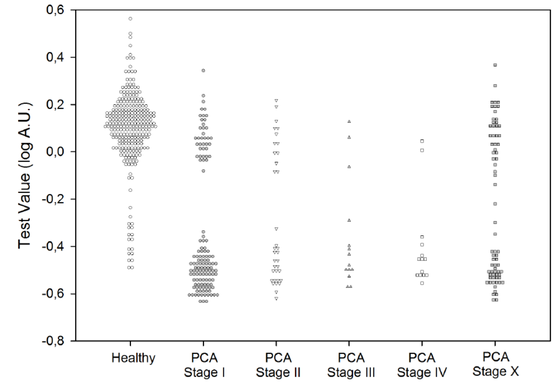
METHODS: We have developed more than 25 ELISA tests for circulating nucleosomes containing different epigenetic features. These assays require 10µl serum and employ a solid phase anti-nucleosome antibody in combination with a labelled antibody directed to bind to a particular epigenetic signal - for example a histone modification, histone isoform, modified cytosine residue or a nucleosome-protein adduct. We have conducted clinical studies in collaboration with clinical centres to investigate these ELISA tests for cancer detection.

EXAMPLE NuQ® ELISA: NuQ®-X



RESULTS
SINGLE SERUM NUCLEOSOME BIOMARKER IN PROSTATE CANCER

VolitionRx has performed a retrospective study on blood samples collected from 537 patients, including 266 men with prostate cancer and 271 age-matched healthy controls, and analysed the samples with a single serum NuQ® adduct biomarker ELISA assay.



Disease stage	Sensitivity at 93% specificity
Stage I	71% (93/131)
Stage II	63% (22/35)
Stage III	79% (11/14)
Stage IV	86% (12/14)

CONCLUSION: A single serum NuQ® adduct biomarker ELISA assay using 10µL serum in duplicate has superior accuracy for detection of prostate cancer than PSA testing. The accuracy of the test may be further improved by use in combination with PSA and this will be a focus of future studies.

RESULTS
PANEL NUCLEOSOME BIOMARKERS IN NSCLC, CRC & PC

NSCLC: A study of 73 patients conducted with Liege University Hospital, Belgium, showed that a panel of 4 epigenetic nucleosome assays combined with smoking history detected 93% of NSCLC cases, with 91% specificity and differentiated NSCLC and COPD.

COLORECTAL CANCER: A collaborative study of 121 patients referred for colonoscopy at the CHU Dinant Godinne - UCL Namur, Belgium found that a panel test of five epigenetic nucleosome biomarker assays detected 87% of colorectal cancer cases and 67% of dysplastic polyps at 90% specificity.

PANCREATIC CANCER: A 59 subject collaborative study with Lund University, Sweden, found that a panel of 4 epigenetic nucleosome ELISA assays and CA19-9 detected 92% of stage II pancreatic cancer cases, with 100% specificity among healthy subjects and 2 false positives among patients with benign pancreatic disease.

CONCLUSION: Epigenetic profiling of circulating nucleosomes using simple ELISA methods offers a biomarker opportunity for the early detection of a variety of cancers.

VOLITION RX