A NOVEL EPIGENETIC IMMUNOASSAY APPROACH TO PROFILING CIRCULATING NUCLEOSOMES FOR COLORECTAL CANCER

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BACKGROUND

Immunohistochemistry studies show genome-wide epigenetic changes in the chromatin of cancer tissue and have identified histo-oncoproteins - histone modifications and other epigenetic changes linked to cancer.

Nucleosome bound DNA fragments contain mutations found in cancer tissue suggesting a tumor chromatin origin for, at least some, circulating nucleosomes. Profiling global levels of epigenetic alterations in circulating nucleosomes can provide disease specific diagnostic information.

The success of stool based screening for CRC adopted across Europe has placed significant strain on colonoscopy capacity.

The aim of the study was to evaluate combined Nu.Q™ blood score and numeric FIT score as a triage approach for positive Fecal Immune Tests in an average risk population i.e. to identify individuals with low risk adenomas or no findings on colonoscopy.

METHODS

In collaboration with the Hvidovre Hospital, University of Copenhagen, serum samples were collected from a training cohort consisting of 1907 FIT positive individuals with colonoscopic confirmation of diagnosis. 10µl serum samples were analyzed using Nu.Q™ ELISA blood tests and an algorithm developed by Linear Discriminant Analysis (LDA) was used to identify individuals with no evidence of cancer.

CONCLUSION & PERSPECTIVE

A single, age adjusted, Nu.Q™ blood test with FIT score could reduce non screen-relevant colonoscopies in FIT positive individuals with minimal reduction in cancer detection. This test could reduce unnecessary colonoscopies and ease pressure on colonoscopy capacity or, alternatively, detect more cancers by increasing the throughput of screened subjects.

Volition Nu.Q™ ELISA

Volition has developed five patent-protected families of Nu.Q™ sandwich ELISA assays, each of which captures intact nucleosomes and labels (identifies) a specific structural feature:

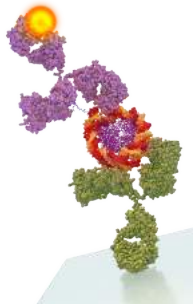
Nu.Q™-X specific DNA modifications

Nu.Q™-V histone variants

Nu.Q™-M histone modifications

Nu.Q™-A nucleosome-protein adducts

Nu.Q™-T total nucleosomes



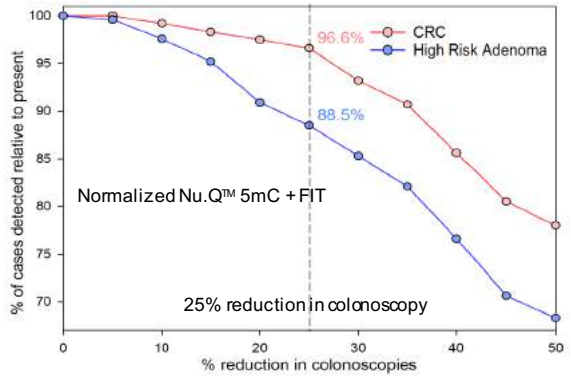
Demographic of the study group

The study comprised 1907 individuals aged 50 to 75 years with average risk and no prior colonoscopy who tested FIT positive for in Danish colorectal cancer screening program.

Patients were classified into 3 groups by colonoscopy result.

Diagnosis	No. of patient	Mean Age	Male:Female
CRC	118	67,3	68:50
stage I-II	72	67,4	40:32
stage III-IV	46	67,2	28:18
Adenoma	989	64,9	691:298
High Risk Adenoma	252	66,3	173:79
Others Adenoma	737	64,4	518:219
Clean Bowel	800	62,2	406:394
Total	1907	63,9	1165:742

Reduction in Colonoscopies vs. test Sensitivity



Potential increase in programme sensitivity