

# NUCLEOSOMICS®

an advanced blood based diagnostic technology for cancer

## INTRODUCTION

Cancer is a leading cause of mortality worldwide, accounting for approximately 13% of global deaths annually. Despite advances in therapeutics the most reliable curative approach to cancer is surgery. However, many cancers are diagnosed at a relatively late stage when they are well established and may have spread beyond the primary tumour. This is in part due to a lack of effective diagnostics. VolitionRx is developing its Nucleosomics® technology platform to identify signatures of nucleosomes - units of the chromosome consisting of short strands of DNA wrapped around packaging proteins. Nucleosomes are released into the blood as cells die and thus represent early diagnostic opportunities for diseases with high turnover, such as cancer.

## HOW IT WORKS

### Nucleosomes: the basic repeat element of chromatin

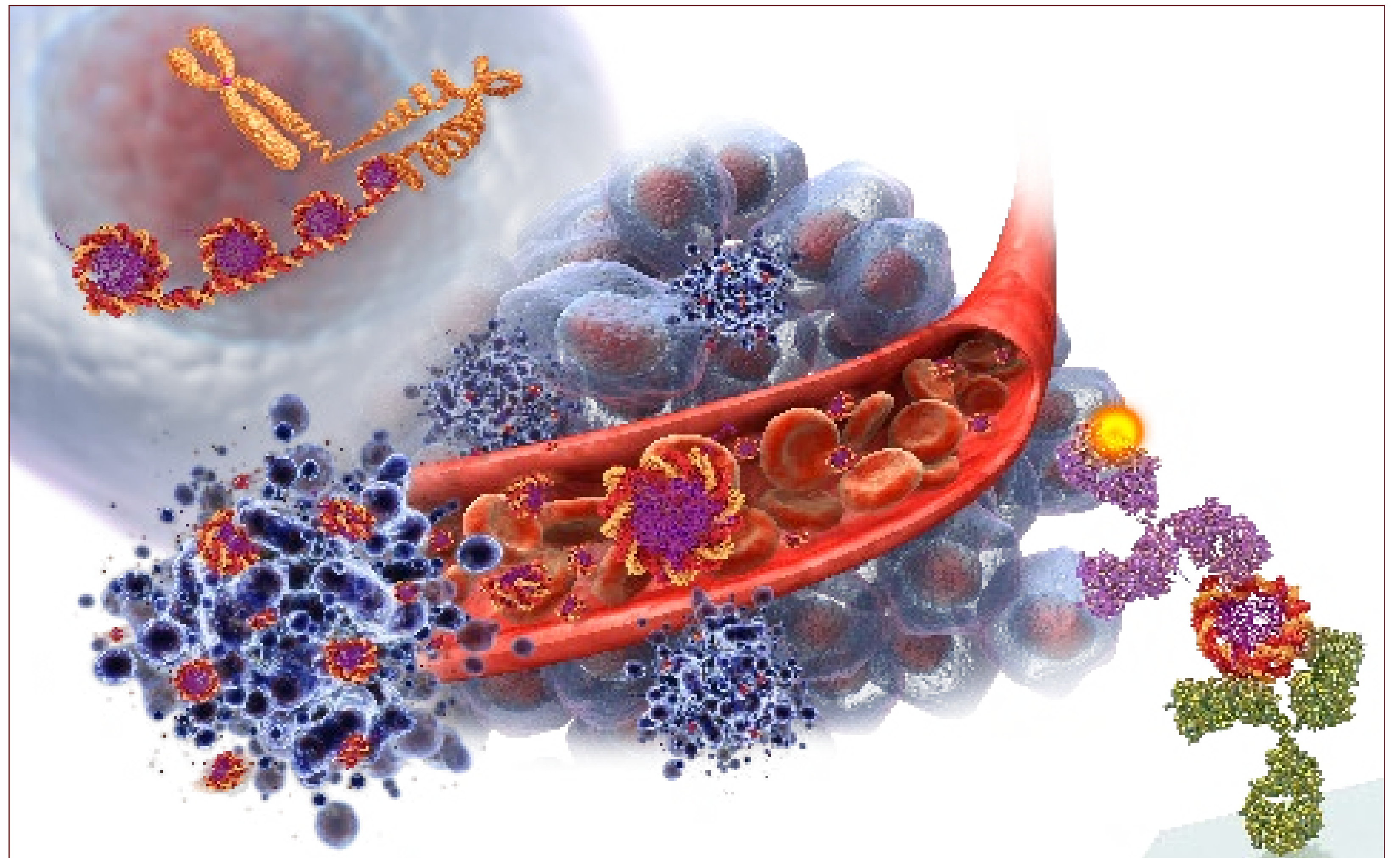
- Nuclear DNA is compacted as protein complexes in a “beads on a string” structure.
- Each “bead” is called a nucleosome, and consists of DNA wrapped around a core of histone proteins (octamer of histone: H2A, H2B, H3 and H4.)
- Histones and the DNA are subject to a variety of post translational modifications.
- Different histone variants also exist.
- Various proteins also interact with nucleosomes.

### Nucleosome and apoptose

- Cell death results in fragmentation and release of nucleosomes into the blood.
- In cancer, high cell turnover results in large amounts of cell debris, overwhelming the recycling mechanisms and leading to elevated blood nucleosome levels.

### Nucleosomics®

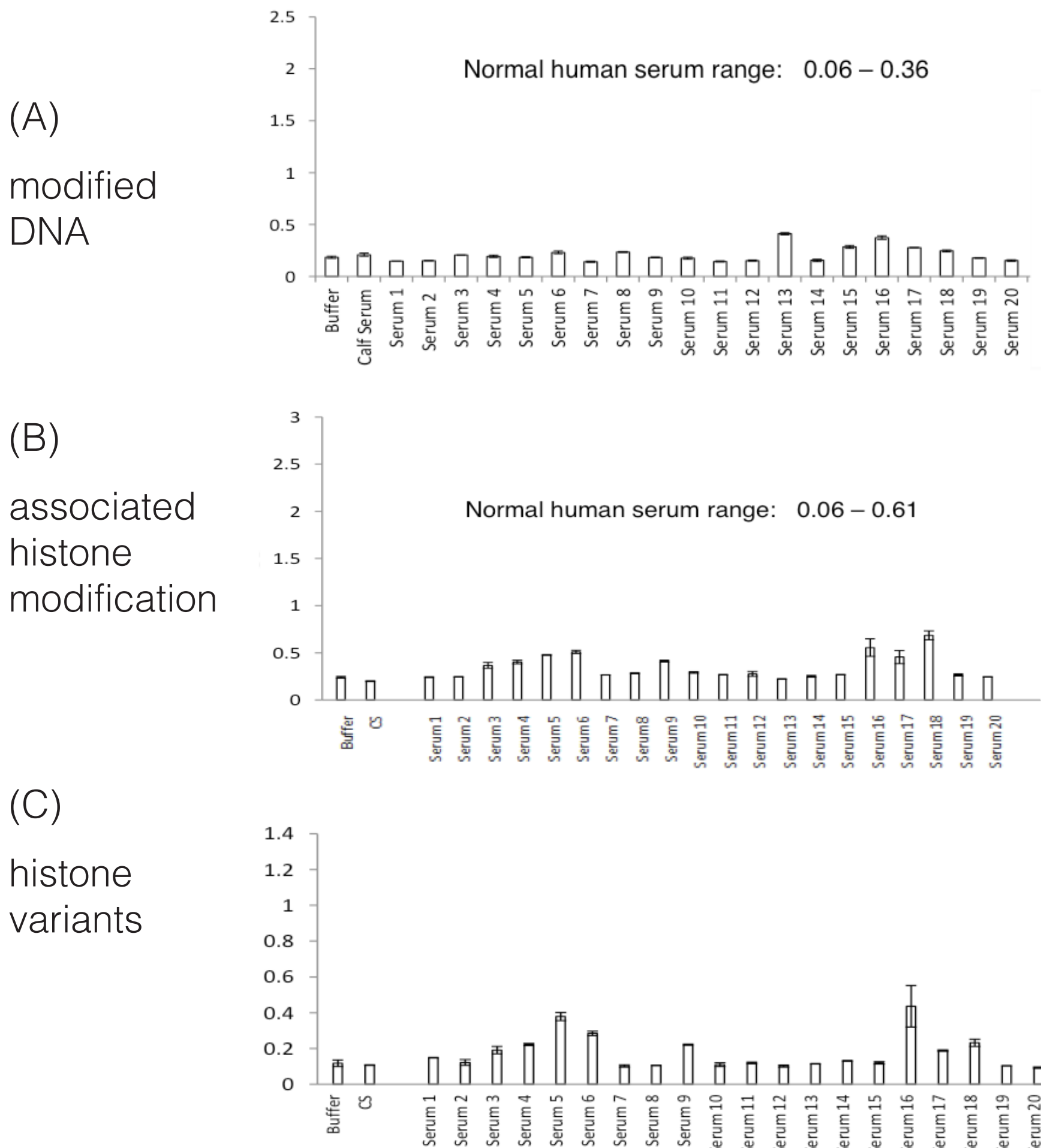
- Nucleosomics® combines these findings to detect the quantity and type/s of nucleosomes present in the blood.
- Each NuQ® ELISA captures intact nucleosomes and labels a specific feature.



## RESULTS: PILOT STUDY

Figure 1: Low nucleosome levels in healthy subjects

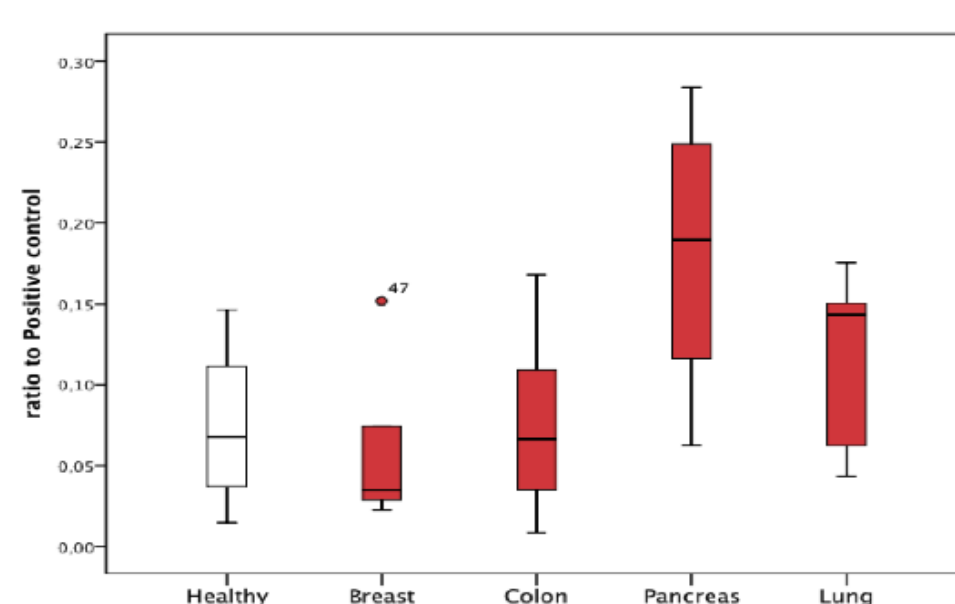
A low nucleosome associated level of:



was detected for serum samples from 20 healthy volunteers using NuQ-X®, NuQ-M® or NuQ-V® kits, respectively.

Figure 2: Pilot study: diagnostic relevance of NuQ® ELISA assays

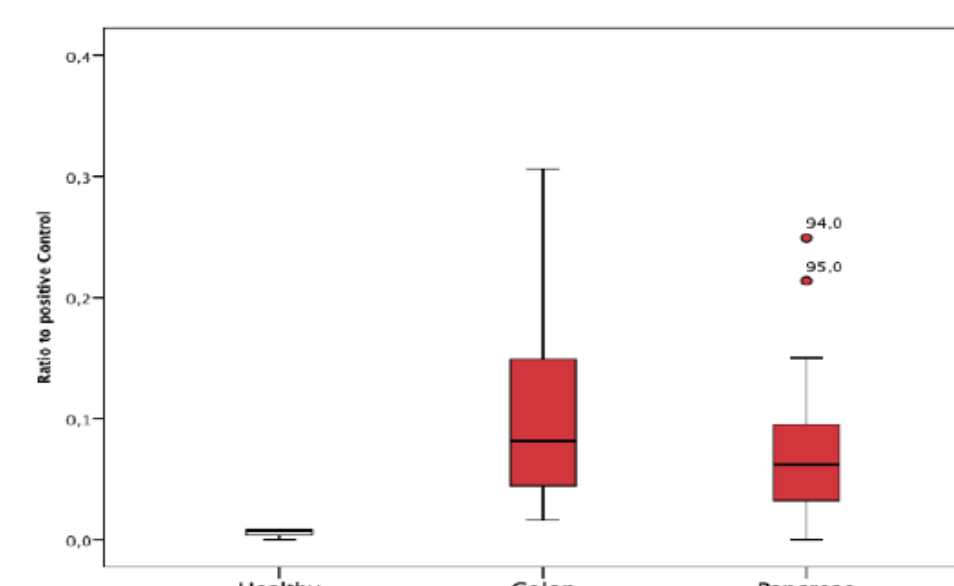
(A) The NuQ-X® assay detected a particularly high level of nucleosomes associated with modified DNA in serum samples from patients with pancreatic or lung cancer compared to healthy subjects.



## RESULTS CONT'D

Figure 2: Pilot study: diagnostic relevance of NuQ® ELISA assays (cont'd)

(B) The NuQ-A® assay detected a high level of nucleosome associated protein in serum samples from patients with colon or pancreatic cancer compared to healthy subjects.



(C) A combination of different NuQ® assays might allow detection of cancer and cancer type. Here, results of a pilot study using NuQ-X® and a NuQ-V® kits on breast, colon, pancreatic and lung cancer. Results are represented as a ratio NuQ-X®/NuQ-V®.

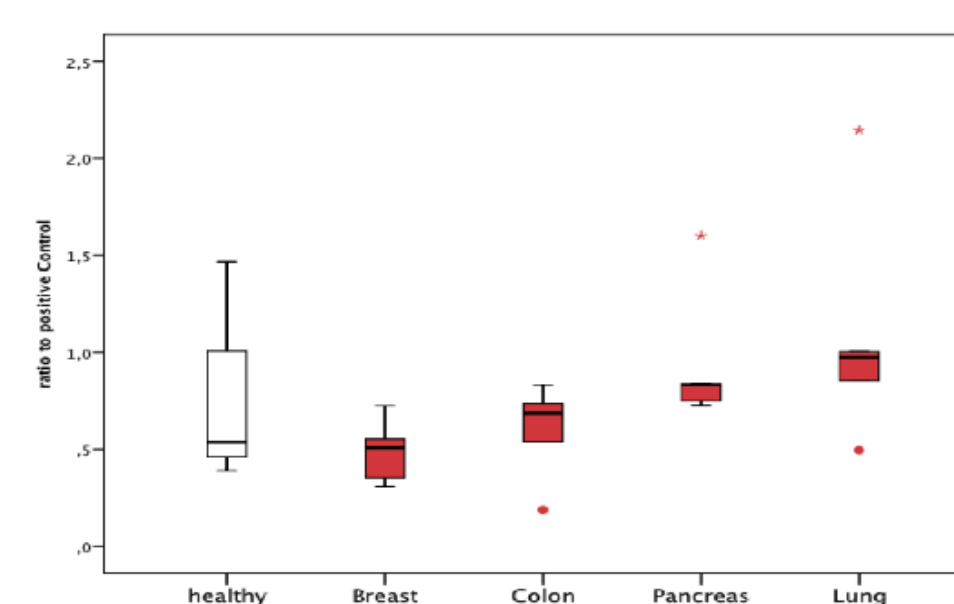
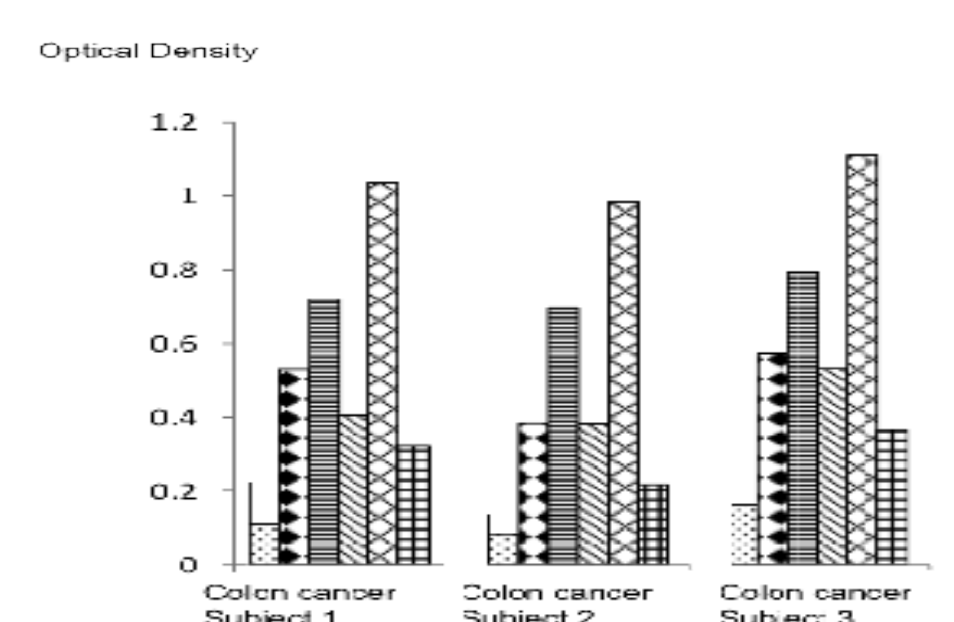


Figure 3: Determination of the nucleosome profile for each cancer type

Example of the nucleosome profile for colorectal cancer using 5 NuQ® assays.



## ACKNOWLEDGMENTS

With thanks to the Government of the Wallonia Region (Région Wallonne), Belgium, for its financial support for Volition's research programme.

## HOW WILL IT BE USED?

VolitionRx has a range of blood-based epigenetic Nucleosomics® tests for different types of nucleosomes and has conducted small pilot studies:

1. to investigate whether these nucleosomes are present in the blood of cancer patients; and
2. to detect the nucleosome patterns that are specific to some cancer types.

Nucleosomics® includes 5 families of tests:

- **NuQ®** Test for the detection of total quantity of nucleosomes in the blood.
- **NuQ-X®** Tests for the detection of nucleosomes containing specific nucleotides (e.g. methylated DNA.)
- **NuQ-V®** Tests for the detection of nucleosomes containing specific histone variants which identify the type of cancer present.
- **NuQ-M®** Test for the detection of nucleosomes containing modified histones which can be used as a blood test for individual cancer types.
- **NuQ-A™** Test for the detection of nucleosome-protein adducts.

## COLLABORATIONS

VolitionRx is currently seeking collaborations with hospitals and biobanks with well-annotated blood samples, from patients with cancer and competing conditions, as well as healthy patients. If you are interested in collaborating with VolitionRx, please contact either:

Marielle Herzog (Lead Scientist) at [m.herzog@volitionrx.com](mailto:m.herzog@volitionrx.com); or

Mark Eccleston (External Collaborations Manager) [m.eccleston@volitionrx.com](mailto:m.eccleston@volitionrx.com).