Volition
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Revolutionizing the way cancer is diagnosed

Volition, a life sciences company, has developed an array of simple blood tests to improve the detection of a wide range of cancers at early stages, with the goal of dramatically improving survival rates in patients.

Cancer is a leading cause of mortality, accounting for approximately 13% of deaths each year worldwide. Despite advances in therapeutics, surgery remains the most reliable way to cure the disease. Unfortunately, many patients are diagnosed too late for this option, at a point when their cancer has already spread. More accurate diagnostic tools are sorely needed to detect cancer at early stages, thereby improving outcomes for patients.

To address this need, Volition has developed an array of non-invasive, accurate and cost-effective blood-based biomarker assays that can be combined in panels to diagnose a wide range of cancers.

The human genome contains 3 billion base pairs, resulting in nearly 2 meters of DNA in each cell. DNA is structured by proteins first into nucleosomes (units of 147 base pairs wrapped around 8 histone proteins) then chromatin and chromosomes. When cells die, millions of nucleosomes are released into the blood. This is the major source of cell-free DNA, only a tiny fraction of which contains specific sequence changes (genetic point mutations).

Volition's revolutionary and patent-protected Nucleosomics platform measures and identifies global changes in the large pool of nucleosomes rather than in the tiny fraction of mutated DNA. Searching for a vanishingly small specific mutation using next-generation sequencing approaches requires much larger volumes of blood and sophisticated, time-consuming analytical approaches. The quantity and characteristics of nucleosomes differ between cancer cells and normal cells, as well as between different types of cancer cells, even at early disease stages. Volition's Nu.Q biomarker assays capture the nucleosomes and generate a colored signal if specific epigenetic alterations are present (**Fig. 1**).

A key advantage of Nu.Q is that it could be easily incorporated into routine blood testing as part of a general health screen carried out by primary care physicians. Moreover, this simple test could be implemented in developing countries where high-tech sequencing equipment is less accessible, and the results could be analyzed automatically using standard equipment at hospital laboratories.

"We think of it as a high-tech application of a low-tech solution," said Mark Eccleston, Volition's business development director. "Our goal is to make the tests as common and easy to use, for both patients and doctors, as existing diabetic and cholesterol blood tests."

Innovative assays

Nucleosomes inside diseased cells are characterized by unique epigenetic signatures—factors that affect gene activity without altering the DNA sequence.

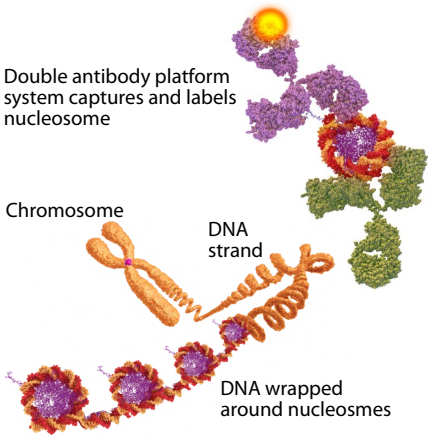

Figure 1: Diagnosing cancer by epigenetic profiling of cell-free nucleosomes.

For example, cancer cells contain nucleosomes with unusual patterns of histone modifications, DNA modifications, DNA methylation, and protein adducts. Moreover, cancer cells turn over more frequently than normal cells, releasing a greater quantity of nucleosomes into the blood as they die.

This higher abundance of nucleosomes means that Volition's Nu.Q immunoassays can quantify and identify disease-associated nucleosomes using only a drop of blood. Four or five assays for a range of modified histones, nucleotides, specific histone variants, and protein adducts can be combined to form a panel test for detecting specific diseases. The successful development of accurate diagnostic tests for a wide range of cancer types could have a major impact on public health.

Catching colorectal cancer

Tackling colorectal cancer and reducing the number of related deaths requires early diagnosis. Although screening can reduce the number of deaths from colorectal cancer by up to 16%, higher compliance and improved test performance, particularly for detecting precancerous polyps—the precursor to colorectal cancer—could significantly improve survival rates.

Screening efforts in the UK and across Europe currently rely on unappealing fecal immunochemical tests (FITs), which have achieved compliance in only 57% of the intended demographic. Moreover, the high percentage of false positives in FITs has resulted in long wait times for expensive follow-up colonoscopies, increasing anxiety among patients and putting a strain on health care systems.

To address this problem, in 2016, Volition developed and CE marked an accurate, patient-friendly Nu.Q Colorectal Cancer Screening Triage blood test. The Nu.Q test combines levels of nucleosomes containing methylated DNA (normalized to the total level of nucleosomes) with numeric FIT score and patient age using a proprietary algorithm to identify individuals with no evidence of cancer and so reduce non-screen-relevant colonoscopies. A trial of 7,944 individuals at average risk for colorectal cancer who had positive FIT screens showed a potential reduction of 24.5% in colonoscopies, with 95% sensitivity for colorectal cancer[1].

A front-line screening test for colorectal cancer is in development, as well as a standalone diagnostic test for patients presenting with symptoms of colorectal cancer. This diagnostic test, which is at the most advanced stage of development, has demonstrated greater than 85% sensitivity for early-stage cancer, picks up approximately three-quarters of precursor polyps, and detects early- and late-stage disease with similar accuracy.

"If precancerous polyps can be detected in a screening program, they can be removed with relative ease, thereby removing that risk of developing colorectal cancer and reducing the actual incidence of the disease," Eccleston said. "By improving detection rates at early stages, our Nu.Q-based colorectal cancer blood test could dramatically improve patient outcomes and save the health care system a substantial amount of money."

Ultimately, this blood test could replace stool-based tests and possibly colonoscopies in high-risk individuals who have not complied with screening efforts.

"The introduction of the blood test for colorectal cancer, and ultimately other diseases, would be the first step towards screening programs with massive public health benefit," Eccleston said. "By increasing screening compliance and radically improving diagnostic accuracy, our revolutionary technology will lead to earlier and more accurate detection of disease at its most treatable stage, allowing more effective intervention and better patient outcomes."

1. Herzog, M. *et al*. Poster presented at DDW, Chicago, Illinois, USA, May 9, 2017.

contact
Mark Eccleston,
Business Development Director
Volition
Namur, Belgium
Tel: +44 (0)7812 046749
Email: m.eccleston@volitionrx.com