A Novel Biomarker-Based Prostate Screening Method to Reduce Unnecessary Biopsies

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Prostate cancer is the second most common cancer in men worldwide, and the fourth overall, according to the World Cancer Research Fund. In 2020, there were more than 1.4 million new cases, and prostate cancer was responsible for over 375,000 deaths. Currently, routine screening involves a blood test to check prostate-specific antigen (PSA) levels. This screening aims to identify patients early, allowing timely intervention and improved patient outcomes, but the PSA test is known to generate very high numbers of false positives, leading to unnecessary biopsies and anxiety for those affected. Researchers have therefore been developing a novel method – based on measuring telomere associated variables (TAVs) in conjunction with PSA – as a more accurate screening tool for prostate cancer, improving risk stratification of suspected cases.

Current Screening Limitations

Cancer screening programs aim to identify patients with early-stage cancer before symptoms appear, allowing timely interventions to improve prognoses and survival rates. The current method for screening patients for prostate cancer risk is to measure their PSA levels, referring individuals with high concentrations for a biopsy. This procedure is not only invasive, painful and costly, it is often unnecessary. In fact, over two thirds of men who undergo a biopsy do not actually have cancer, and so have been subjected to an uncomfortable procedure unnecessarily [1]. Furthermore, research suggests that PSA screening does not actually prevent cancer deaths, and it is not an accurate predictor of cancer risk on its own [2]. There is therefore a clear need to develop better testing methods that can identify cancer risk more accurately.

Identifying New Biomarkers for Prostate Cancer

Telomeres are regions of repetitive DNA sequences found at the ends of chromosomes that protect them from becoming frayed or tangled. Telomere length has been identified as a promising biomarker for cancer risk, with abnormal or accelerated shortening of telomeres linked to increased risk of malignancy across a number of different cancers [3]. This concept was studied in the Horizon 2020-funded ONCOCHECK project, in which the Spanish biotech company Life Length aimed to clinically validate TAVs as a biomarker for both haematological and solid tumours. The project was particularly successful at identifying lung and prostate cancers, the latter study involving 1,200 men who all underwent prostate biopsies. The cohort demonstrated improved diagnoses overall, allowing the company to develop highly precise and predictive algorithms to determine a patient's risk of having prostate cancer.

Developing a Better Test

These algorithms have been developed into ProsTAV®, a state-of-the-art *in vitro* diagnostic assay to identify patients with an elevated risk of suffering from aggressive prostate cancer. Analysis of a range of data sets – including a patient's age, PSA level, digital rectal examination results and TAVs – generates a prostate cancer risk score between zero and 100. The patient's urologist can then use this score, as well as other screening factors, to decide whether to refer them for a biopsy.

The company has invested in a number of laboratory automation solutions to increase efficiency, scale up its testing capabilities and accelerate its workflow. All the assays are now prepared on either Fluent® or Freedom EVO® liquid handling platforms (Tecan), allowing the company to automate many of its complex tasks.

For example, the workflow requires the removal of cellular membranes in a series of wash steps, and this delicate procedure has been safely automated on the Tecan instruments to avoid damage to the chromosomes. Furthermore, the 384-channel pipetting head of the Fluent platform's Multiple Channel Arm™ provides greater repeatability compared to manual or even semi-automated methods, while the Freedom EVOware® Sample Tracking software delivers end-to-end traceability for each sample prepared on the Freedom EVO platform. These technologies have enabled the company to increase the number of samples processed per day, improving throughput while being sure that samples are accurately processed and linked back to the correct patient.

Stephen J. Matlin, CEO of Life Length, commented: "The objective of ProsTAV is to reduce the number of unnecessary biopsies in men with elevated PSA levels. PSA testing leads to almost two million prostate biopsies a year, of which around 1.4 million end up testing negative. This highlights how inefficient PSA testing is; it frequently leads to extremely unpleasant biopsy procedures being performed on men that do not actually need it. We want to eliminate a significant number of these biopsies by replacing them with a combination of tests, including our sensitive telomere-based method. Now that our workflow has the precision and flexibility afforded by our Tecan platforms, we are aiming to become an essential service for urologists wanting to improve their diagnostic procedures."

The Future of Prostate Cancer Screening

The need for a better screening method for prostate cancer is well known in the medical community, as the current approach of PSA testing frequently leads to unpleasant prostate biopsies being performed on men who do not necessarily need them. TAVs have been shown to be an effective biomarker for identifying prostate cancer and could be used in combination with other screening methods to help triage patients in need of further examination. This new assay provides an opportunity to reduce the number of prostate biopsies by more than a third, eliminating many unnecessary procedures. This will generate a significant clinical benefit for patients, as well as providing substantial economic savings for both public and private healthcare systems.

References

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