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OTraces Plans Early Cancer Diagnostics Based on Signal-Enhanced Protein Markers

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Premium

NEW YORK (GenomeWeb) – Despite commercial attempts to develop noninvasive molecular tests that could serve as sentinels against the earliest signs of a developing cancer, there is still little data demonstrating that the most popular strategy— detecting changes in circulating DNA — is possible, let alone practical.

But according to a firm called OTraces, DNA may not be necessary for the sensitive detection of early cancers, at least in some cases. Instead, the company is developing cancer screening tests based on a mathematic strategy of enhancing signals and suppressing noise for a collection of well-known and relatively well-characterized proteins.

Although OTraces has not published any data yet that supports these claims, the firm's CEO Keith Lingenfelter said this week that assays the firm is currently validating can distinguish patients with prostate or breast cancer more accurately than currently used screening tools — prostate specific antigen (PSA) and mammography, respectively.

The company believes the approach can also differentiate between aggressive and non-aggressive tumors, determine cancer stage, and track progression.

Assays the company is developing for these two cancer types both rely on the analysis of a group of proteins in blood that the firm says offer a proxy for activity that takes place between tumors, their immediate environment, and the immune system — also known as the tumor microenvironment, or TME.

Straight analysis of these biomarkers is a poor strategy for cancer detection because they are wildly unspecific, rising and falling in a variety of different disease states, or based on physiologic changes that have nothing to do with cancer, Lingenfelter said.

According to Lingenfelter, OTraces has overcome this issue by creating proprietary strategies to pull out a cancer-specific signal from the background noise of circulating proteins. The method combines two

computational strategies that OTraces has patented — steps it calls proteomic noise suppression and multidimensional spatial correlation.

The approach uses mathematical methods determine how a particular individual patient's results compare to population averages on several different metrics and in multiple dimensions, and is described in detail in a white paper on the firm's website.

These mathematical strategies allow OTraces company to isolate certain protein signatures that represent the tumor microenvironment from the complex background of other blood-borne molecules.

The principle is simple. If you can detect evidence of a tumor microenvironment, arguably, there is a tumor. In addition, Lingenfelter said, measuring changes in these signatures can offer information on cancer aggressiveness, progression, and the activity of the human immune system against a cancer.

Aside from the mathematical aspects of the approach, the test strategy is mundane, and inexpensive: sandwich immunoassays for the various protein targets supply the base readout, which include IL6, TNFα, IL8, and VEGF.

OTraces has been validating a breast cancer screen based on these markers in Russia, using the proteomic noise suppression methods the company has developed.

Though it has not published this data in a peer-reviewed journal, OTraces said that it has applied its approach to a cohort of 200 women diagnosed with breast cancer via mammography and biopsy, as well as a group of controls, in collaboration with the Gertsen Institute in Moscow.

According to the company, retrospective analysis based on the women's clinical diagnoses showed that the test performed with over 95 percent predictive power, including in stage 0 and stage 1 tumors.

The firm believes it has an easier commercial path for the breast cancer test in Russia, due to local demand for a less expensive alternative to mammograms. But Lingenfelter said that the ultimate goal is to also launch the assay in the US.

In prostate cancer, the company has been validating a test with researchers from Johns Hopkins University, led by Kenneth Pienta.

According to OTraces, validation work completed so far shows the tumor microenvironment protein signature has a 90 percent predictive power in separating aggressive prostate cancer from cancer-free samples.

Lingenfelter said that the company sees a more immediately receptive environment in North America for prostate cancer, in light of widespread frustration with the lack of specificity of PSA tests.

According to OTraces, current PSA assays offer about 90 percent sensitivity but sacrifice specificity, which is closer to 50 percent. The OTraces method, at least as described by the company, reaches 95 percent sensitivity and 90 percent specificity.

In promotional materials, OTraces has sought to define itself in relation to the larger liquid biopsy market, which includes a number of firms that have focused on DNA sequencing, but also others that are exploring so-far undescribed approaches based on machine learning and other computational methods, which could potentially involve a range of biomarkers beyond DNA or RNA.

Companies like Grail and Freenome have tasked themselves with developing highly sensitive and specific pan-cancer screening tests — the kind of assays that could potentially be applied population-wide.

OTraces, at least so far, appears to be in much more direct competition with the specific tests it is posing itself to displace — PSA and mammography — as well as some of the other assays that have been advanced in recent years with the same goal.

Lingenfelter said that OTraces intends to launch a prostate cancer screening test in North America for the detection of prostate cancer in otherwise healthy men that would be a true replacement for PSA, but that will require a large trial involving thousands of men for full regulatory review.

In the nearer term, he said, the company believes it can go to market with an LDT for determining prostate cancer aggressiveness in men who have high PSA levels and other clinical signs that indicate cancer, to help doctors determine how to proceed with their care.

"It's a huge unmet medical need, what do you do with men with low-grade prostate cancer … so we can probably market this as a CLIA lab test, an LDT, and the plan is to be on the market in six to eight months," Lingenfelter said.

Competitors to such an assay include firms like MDNA, which has developed a blood-based PCR test that measures alterations in mitochondrial DNA, and claims 87 percent sensitivity and a 97 percent negative predictive value in distinguishing men with Gleason score-7 or higher prostate cancers.

German firm Chronix Biomedical has reported that its circulating DNA-based test can discriminate prostate cancer from controls with an area under the receiver operating curve (AUC) of .92, representing a diagnostic accuracy of 83 percent.

MDxHealth, which recently launched a noninvasive prostate cancer test called SelectMDx, has reported an AUC of 0.89.

Meanwhile, the company is advancing its breast cancer screening assay in Russia, but with the hope that it can then translate it to the US market as well. "Trying to get a screening test up against the entrenched mammography is a greater task," Lingenfelter explained.

The firm also has data, he said, that the same mathematical approach to analyzing TME-associated cytokines could screen for a variety of other tumor types, but it has not released any data on that yet.

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