MiR Diagnostics Advances Non-Coding RNA Test for Prostate Cancer Classification

Jun 11, 2015 | a GenomeWeb staff reporter

Premium

NEW YORK (GenomeWeb) – Startup MiR Diagnostics has begun laying the groundwork for a prospective study to validate its ncRNA-based test for differentiating indolent from aggressive prostate tumors, with the goal of launching the diagnostic in mid- to late 2018.

The study is expected to evaluate the test's performance in tumor samples obtained from up to 2,000 patients at multiple clinical centers in the US, company Co-founder and CSO Martin Tenniswood told GenomeWeb.

Based on a positive outcome of the study, as well as discussions with the US Food and Drug Administration, MiR could begin marketing the test in about three years, CEO Sam Salman added.

Founded in 2012, MiR is focused on developing and commercializing discoveries made in Tenniswood's lab at the University of Albany, where he has been researching gene expression in prostate cancer for decades.

A significant portion of that work relates to identifying new biomarkers for the classification of prostate tumors — an area of significant unmet need, according to Tenniswood.

While blood tests for prostate-specific antigen (PSA) are effective for identifying men with prostate cancer, "PSA levels are not, in any way, prognostic as to whether or not you have a cancer that needs treatment or a cancer that does not," he explained.

Prostate cancers are frequently slow-moving and are usually diagnosed in men in their late 60s or early 70s. In these cases, treatment — typically prostatectomy or radiation therapy — is unnecessary. Yet identifying the estimated 70 percent of prostate cancer patients who do not require intervention remains challenging.

If a patient is diagnosed with apparent prostate cancer following a digital rectal exam or a transrectal ultrasound, a 12-core needle biopsy is performed. The tissue samples then undergo histopathological analysis and are assigned a grade — known as a Gleason score — that reflects the tumor's likelihood of

spreading.

In a large percentage of cases, Gleason scores fall somewhere in the middle of ranking system's 2 to 10 range and are difficult to characterize with any certainty. As a result, "we're overtreating prostate cancer to the level of about $1.3 billion a year," Tenniswood said. "That's an enormous burden on the healthcare system."

Aiming to provide a better alternative to Gleason scoring, Tenniswood and collaborators began looking at whether miRNAs could be used to more accurately identify which prostate cancer patients had aggressive tumors and required treatment.

They developed a method for consistently and reproducibly extracting non-coding RNAs from standard formalin-fixed, paraffin-embedded core needle biopsy samples and then analyzed them using Affymetrix's GeneChip miRNA 3.0 array, he explained.

They discovered that expression patterns for a number of miRNAs, as well as some small nucleolar RNAs, could be correlated to prostate tumor samples that had been graded with different Gleason scores.

The researchers then developed an algorithm designed to individually evaluate each of the roughly 3,000 ncRNAs on the Affymetrix array so as to determine their prognostic value independent of Gleason score or PSA levels.

Using this approach, Tenniswood and his team identified 56 miRNAs and snoRNAs, which remain undisclosed, that are expressed at significantly different levels in aggressive tumors versus indolent ones. A tumor was deemed aggressive if the patient eventually experienced biochemical failure — a rise in PSA levels after prostatectomy or radiation therapy.

Tenniswood said that MiR has transferred the test onto an RT-PCR platform based on Life Technologies' OpenArray technology, which he said enables the company to analyze a large number of patient samples at one time.

To help validate the test, MiR analyzed a set of biopsy samples from 17 prostate cancer patients whose disease outcomes were kept secret. Two of the tumors were deemed aggressive, 11 were considered indolent, and four ruled "suspicious."

When the samples were unblinded, the company found that it had correctly classified all aggressive tumors, but wrongly ruled one indolent tumor as aggressive. To Tenniswood, however, this specificity misstep is not an issue.

"What's important is that we haven't missed any aggressive patients," he said. Based on the test's performance in this small study, less than 10 percent of patients would be overdiagnosed — a significant improvement over current approaches.

Noting that these findings, while promising, are very preliminary, Tenniswood said that MiR is now in the process of collecting and analyzing data from a recently completed retrospective study of 300 prostate cancer patients.

The company has also partnered with the first of the multiple medical centers it aims to work with on a large prospective study involving up to 2,000 patients, he said. Given that the company only needs to confirm which patients have aggressive disease, Tenniswood said he anticipates obtaining definitive data from the trial in about three years.

In the meantime, Salman said that MiR is working to educate clinicians about the potential value in alternative methods of classifying prostate tumors and is in negotiations with the University of Albany to secure the intellectual property rights to Tenniswood's research.

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