Prominex Developing Rapid Point-of-Care MDx Using Novel Detection Tech

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NEW YORK (GenomeWeb) – With novel amplification and detection technology, startup Prominex promises fully-automated multiplex molecular point-of-care testing that can provide results in five minutes.

The firm recently raised $4 million in Series A-1 funding and is driving towards launching a sample-in, results-out, CLIA-waived instrument and infectious disease assays in the next three years for an intended market of hospitals, emergency departments, intensive care units, and physician offices.

The Prominex molecular diagnostics platform, called the Validex System, uses two novel technologies to enhance speed and sensitivity, said Paul Thomas, the firm's CEO, specifically a proprietary coupled hairpin amplification system (CHASE) and waveguide detection technology.

"We can deliver a result — and this is sample-in to answer-out — in five minutes, and it will have the accuracy of a central lab test," Thomas said in an interview.

Prominex was founded by Thomas along with the firm's CTO Mick Becker and CCO Paul Gargan. The three had overlapping careers at Roka Bioscience and Gen-Probe prior to founding San Diego-based Prominex in December 2017, and the firm has been largely in stealth mode until now, according to Thomas.

The CHASE technology uses a thermophillic nuclease mediated amplification that is "a completely new approach" to molecular detection, Gargan said.

Specifically, the front end of the technology incorporates a duplex-specific nuclease (DSN), an enzyme that cleaves double-stranded DNA as well as the DNA in DNA/RNA duplexes.

Derived primarily from the hepatopancreas organ, or tomalley, of a species of king crab called the Kamchatka crab, also known as the Alaskan king crab, DSNs were initially used mostly for cleanup purposes in genomics applications.

For example, the enzyme is used in sequencing applications such as RNA-seq, to enhance the gene discovery rate of a cDNA library in a process called DSN-normalization, and a minor allele enrichment method called nuclease-assisted mutation enrichment using probe overlap (NaME-Pro). However, it has also been used to enable miRNA and SNP detection, as described in a 2015 *Trends in Biotechnology* review.

Mick Becker invented the DSN-based CHASE technology while still at Roka Bio, in part by finding a novel use for this enzyme. In the Prominex application, the DSN is used in combination with two hairpin oligonucleotides, explained Gargan.

A reporter hairpin has a fluorophore and quencher in close proximity on the tip of its stem, such that, "When the stem is intact there is no fluorescence from the molecule," Gargan

said. The other hairpin is dubbed the trigger. When it interacts with a target molecule, the loop of the hairpin opens up.

"The duplex-specific nuclease that we are using then essentially digests away the DNA portion of the target-loop complex and releases the stem from that trigger hairpin," Gargan said.

This stem portion is designed to bind to the loop of the reporter hairpin, popping it open and separating the quencher from the fluorophore. The DSN then recognizes the hybrid DNA/RNA loop structure and digests and releases the two stems, Gargan said.

"In the presence of a target, we get a billion-fold release of fluorescently labeled oligonucleotides," he said.

On the back end, the released fluorophores are captured on a two-dimensional spatial array of complementary capture oligos. The system then uses a technology called fluorescent waveguide illumination detection, which consists of a plastic structure with a lens that focuses laser light and generates an evanescent wave that excites the captured labeled oligos.

Waveguide detection is about 1,000 times more sensitive than a normal fluorometer, Gargan said, because it only targets what is on the surface.

"The beauty of our technology is we've been able to integrate both of these together, and both our chemistry and our detection technology are sort of agnostic as to the matrix so we can use crude clinical samples," he said.

The technology enables multiplexing in the tens of targets range, and the rapidity of the front-end reaction and detection steps means it can generate results in less than five minutes, according to the company.

Commercialization strategies

That five-minute window is a critical component of an anticipated competitive advantage over current CLIA-waved point-of-care molecular diagnostics, as well as ones that are in development, Thomas said.

In the CLIA-waived POC and near-patient MDx space, the system would need to compete with the Abbott Alere i and the Roche Liat systems, the Mesa Biotech Accula, as well as Cepheid Xpert Xpress. In addition to these waived systems, "there's a whole bunch of folks lined up behind them that have intention to move into the point-of-care space," Thomas noted.

However, none of these current or future competitors can perform an assay in five minutes, he said. Furthermore, the firm has conducted extensive interviews and research with customers, and, based on that feedback, it has determined that test speed is critical.

"Most of the other folks are doing tests in say the 20-minute time frame or longer. ... What we found is, as you move from five minutes out to 30 minutes, people's interest in a test declines dramatically, especially since the average physician office visit is like 10 minutes," Thomas said.

Yet, it is not enough to have a fast test. A test for places like physician offices must also be cost-effective.

Thomas said the firm has not yet set a price for its Validex system, but he noted that the estimated cost to manufacture the instrument is currently less than $1,000 and the disposable assays are between $1 and $2 each.

Of course, rapid immunoassays are also fast and cost-effective, but they often receive criticisms for their accuracy. Molecular tests are typically more sensitive and specific than immunoassay-based testing, but there are no published descriptions of the performance of the Validex system yet.

However, "We have run clinical samples internally, and we're very pleased with the performance of the system," Thomas said.

Prominex has established a relationship with researchers at The Scripps Research Institute, he said, to enable sourcing of clinical samples, collecting user feedback on menu prioritization and user interfaces, and, eventually, help with clinical trials in support of a 510(k) application and CLIA waiver.

The firm is also consulting with leaders in the field of infectious diseases.

Its first assay in development is for chlamydia and gonorrhea testing, while the second will likely be a test for influenza A/B and respiratory syncytial virus. Thomas is cautious in assigning a timeline to the process but said at this point the firm believes it will have its instrument and the first two assays through a 510(k) clearance and CLIA-waiver process within the next three years.

The firm also sees opportunities in other respiratory tract infections, such as Group A Strep, Thomas said.

"Beyond that, there are hospital-acquired infections like [methicillin-resistant *staphylococcus aureus*] and *Clostridium difficile*, there are bloodstream infections — we have a whole list of what we call actionable point-of-care assays that we have lined up for menu development," he said.

The respiratory niche is now populated by CLIA-waived POC molecular flu A/B and RSV assays from Abbott, Roche, and Cepheid, and Cepheid is also leveraging its rapid CT/NG testing at STI clinics like the Dean StreetClinic in London and the Broward County Wellness Center in Florida.

Prominex acquired the intellectual property rights and the assets related to CHASE amplification chemistry from Roka Bio, Thomas said, and simultaneously entered into a license agreement for the waveguide detection technology with mBio Diagnostics. It is also working on instrument development with Invetech, "a global leader in design, development, and manufacture of point-of-care molecular diagnostic systems," he said, with expertise in CLIA-waivable design.

Roka Bioscience, meanwhile, sold its assets to Rokabio, a newly formed subsidiary of the Institute for Environmental Health, a food testing firm, for $17.5 million late last year. As part of the liquidation process, Roka Bioscience then changed its name to Sorrento Tech, according to forms filed with the US Securities and Exchange Commission prior to voluntarily de-listing from the NASDAQ.

At Rokabio and IEH, "there was really no interest in [the CHASE] technology, certainly not in clinical applications. ... The Prominex leadership team was able to initiate a dialog with IEH and extract the rights to this technology in clinical diagnostics and life science applications on a global basis," Thomas said.

Prominex also intends to establish a partnership with a global IVD player for the commercialization of its product upon clearance. "We need to look for someone with the global reach and distribution muscle to be able to take this product into all the various care settings where we think it is going to offer tremendous advantages for patient care as well as for provider economics," Thomas said.