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ALL PROFILES ISSUE

IN VITRO DIAGNOSTICS

Quanterix Corp.

Single molecule immunodiagnostics

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Contact: David Hanlon, Director of Strategic Marketing
Business: Single molecule assays for Alzheimer's disease and prostate cancer
Founded: April 2007
Founders: David Walt, PhD (Tufts University), Nick Naclerio, PhD (Parallele, Motorola)
Employees: 20
Financing to Date: $15 million
Investors: ARCH Venture Partners; Bain Capital Ventures; Flagship Ventures
Board of Directors: Nick Naclerio; David Walt; David Okrongly, PhD, CEO; Keith Crandell (ARCH Venture Partners); James Nahirny (Bain Capital Ventures); Doug Cole, MD (Flagship Ventures)
Scientific Advisory Board: David Walt; Robert Corn, PhD (University of California); Larry Krichka, DPhil (University of Pennsylvania); Michael Ramsey, PhD (University of North Carolina); Sunney Xie, PhD (Harvard University)

Immunodiagnostics is one of the foundational techniques of biotechnology, but it hasn't changed significantly since its invention in the 1970s. **Quanterix Corp.** has applied fiber optic technology to immunodiagnostics to create a dramatic improvement in sensitivity based on single molecule counting. The company intends to use its platform to develop in vitro diagnostics for several clinical applications, beginning with prostate cancer and Alzheimer's disease.

A traditional enzyme-linked immunosorbant assay (ELISA) works by layering an antibody onto a plate surface, followed by the analyte and another antibody that forms a molecular sandwich. The second antibody in turn can be linked to a reporter enzyme, which produces a visual signal by converting a non-fluorescent substrate into a fluorescent product in the final stage of the procedure.

Quanterix's *Single Molecule Array* (*SiMoA*) platform uses the same biochemical elements as ELISA. The major difference in SiMoA, which uses paramagnetic beads as the substrate to construct the molecular sandwich, comes from running the assay such that there are more beads than there are protein molecules in the serum sample. That way, each enzyme label is on an individual paramagnetic bead, but not all beads will have an enzyme attached. After the blood sample containing the protein has been added and the molecular sandwich is built up, the beads are loaded into tiny, individual wells and sealed. Because each bead is trapped in a very small space, the fluorescent product produced builds up a signal in just a few seconds.

All the beads in the array can be analyzed at the same time using a fluorescence microscope and a camera to resolve individual wells that contain beads and enzymes. The apparatus takes pictures every 30 seconds for two minutes after the addition of substrate and sealing. The wells that light up contain analyte, and the concentration of analyte in the sample can be determined by the ratio of analyte-coated beads to the total number of beads. The technique's sensitivity "is basically just a physical consequence of the fact that we're detecting single molecules," says David Okrongly, CEO of Quanterix.

Founder David Walt, a professor of chemistry at Tufts University, also founded Illumina Inc., a leading genomics company. After receiving an initial round of funding, Quanterix quickly demonstrated that the technology could yield up to a 1,000-fold increase in sensitivity compared with existing immunodiagnostics.

Quanterix is currently developing clinical tests in two areas. One program is in Alzheimer's disease. In the US, about a million people a year present to a physician with cognitive impairment, but there can be many explanations for the problem and it may take six months or more to diagnose Alzheimer's. Current in vitro diagnostics are highly invasive, requiring a lumbar puncture to sample proteins in the cerebral spinal fluid. The same proteins can be found in the blood, but at levels well below the limits of detection for current assays. The Quanterix AD test uses three markers, which the company is in the process of validating.

A number of major pharmaceutical companies have programs in neurologic disorders, including Alzheimer's disease, Parkinson's disease, and traumatic brain injury, and Okrongly believes that the Quanterix test can be used to develop blood-based biomarkers for those indications. "That's the Holy Grail, to have a noninvasive tool to measure biomarkers from the brain. Nobody has been able to do that. We think this has a great risk-reward profile," he says.

The company's prostate cancer diagnostic will measure prostate-specific antigen (PSA), a marker used today to monitor men for prostate cancer recurrence. The program is more of a sure thing than the AD test, Okrongly believes. About 70% of patients who undergo radical prostatectomy will have no disease recurrence, but at present physicians have no way to identify those patients, or those who are likely to experience a relapse. Relapse is today defined as the point at which PSA levels rise to a detectable level with today's ELISA technology. The Quanterix PSA antigen test, called *AccuPSA*, will be used to monitor for disease recurrence, because the test's greater sensitivity could provide important benefits. "We believe that by measuring the level of PSA three to six months after surgery, we will be able to demonstrate a strong correlation between the reduction of PSA after surgery and the prognosis for long-term survival without disease. As a second stage, we will run clinical trials to demonstrate the ability of AccuPSA to monitor PSA and detect disease recurrence much earlier than the standard PSA test, which opens up the possibility for a physician to intervene sooner in the disease process," says Okrongly.

Quanterix is finalizing the development of the PSA assay. Quanterix scientists studied 30 prostate cancer patients who had a radical prostatectomy and showed that the SiMoA technology could quantitate PSA levels in all subjects, at levels up to ten thousand times lower than are detectable by

the standard PSA blood test on the market.

The SiMoA technology could find broad application because it uses the same tools as traditional ELISA assays. "All of the antibodies that have ever been generated to do ELISA work are part of the armamentarium for other SiMoA tests. We don't have to invent anything new to go after every animal or human protein that already has antibodies developed for it. People working with ELISA in studying some disease process will now have a much more sensitive tool to detect proteins with those same antibodies," says Okrongly.

He believes that the company can swiftly produce cash flow. "We believe that by applying the technology in a couple of clinically important areas, where we can control the testing and make the tests available through our clinical laboratory, we can create a revenue stream quickly enough to self-fund the company after 2014," says Okrongly.

He expects the first diagnostic tests to be transferred to the Quanterix Clinical Laboratory by the end of this year. The company will soon begin studies of frozen serum prostate cancer specimens to see if the level of the PSA marker soon after surgery successfully predicts absence of disease recurrence five to 10 years later. At the same time, Quanterix intends to license the technology for use outside of in vitro diagnostics, as a life science tool. "That would be a very complementary relationship for us to get into," says Okrongly.

The PSA recurrence testing market is currently about $500 million globally, according to Okrongly. The market size for an AD diagnostic is a bit difficult to predict. There are drugs currently on the market that treat disease symptoms, and it would be beneficial to patients to receive an earlier diagnosis. "The sooner these therapies are given, the more effective they are, so an accurate and early diagnosis is crucial. A successful test for neurodegerative diseases like Alzheimer's would open up a big market, given the scope of the disease worldwide, and the fact that we have a rapidly growing elderly population around the world," says Okrongly.

The market could be dramatically increased by new drugs in development that have the potential to reverse or halt progression of the disease rather than treat symptoms. "Right now the best we can do is treat symptoms. If any of these new disease-altering therapies become FDA approved, then it becomes a huge market. We could potentially provide a test to monitor the efficacy of these therapies," says Okrongly.

He believes that the SiMoA technology represents the next step for ELISA, which in its current form has reached the limit of its potential sensitivity. "It took a quantum leap like single molecule counting to change the paradigm (and dramatically increase sensitivity). Nobody is breaking away from the old paradigm of measuring ensemble label signal in the same way that we are. I liken the arrival of the single molecule approach for immunodiagnostics to the situation when analog electronics gave way to digital electronics."

It's unclear whether or not the company will attract FDA scrutiny. CLIA lab diagnostics have traditionally been outside of FDA's purview, but the agency has indicated of late that it intends to regulate them more thoroughly. Quanterix is proceeding under the assumption of FDA regulation, according to Okrongly. "When I came here, my goal was that regardless of the way the regulatory environment evolved, we would be ready. Our intent is to build our products to a high quality standard, whether they are under FDA purview or not," he says.

The company raised a total of $15 million during Series A financing, with investors that included ARCH Venture Partners, Bain Capital Ventures, and Flagship Ventures.

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— Jim Kling