Rapid, Cost-Effective Diagnostic System Based On Innovative Nano Biosensors Helps Identify And Slow Spread Of Major Diseases

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Throughout history, human migration has contributed greatly to the spread of infectious diseases. Trade caravans, religious pilgrimages and military maneuvers spread many diseases such as influenza, plague and smallpox.

Today, epidemics continue at an accelerated rate thanks to an internationally mobile population with unprecedented access to quick, global travel. This increased international mobility has created the potential for a serious and costly health crisis, prompting world health authorities to seek rapid, high-throughput disease surveillance and reporting programs as a first line of defense. A solution needs to identify, manage and contain highly communicable infectious diseases such as tuberculosis (TB), human immunodeficiency virus (HIV), hepatitis, influenza and severe acute respiratory syndrome (SARS).

Infectious diseases can be separately diagnosed with existing highly effective gold-standard diagnostic tests such as

culture and/or polymerase chain reaction (PCR). But, the most sensitive and accurate tests conducted in clinical labs usually take days to provide an answer, while the very rapid tests that require only a few minutes are usually less sensitive and inaccurate.

Performing individual tests for each of these diseases at a reasonable cost, though, creates formidable logistical and financial challenges. A more innovative solution that cuts down the number of tests is needed.

Next Generation Disease Screening

One possible solution that shows great promise is a high-throughput diagnostic system, which is commercially available from Akonni Biosystems, a private molecular diagnostic company based in Frederick, Md. Called TruSentry, the system can extract DNA and/or RNA directly from either a tiny spot of dried blood or whole blood and then subject the single sample to testing for 10 to 20 of the most prevalent diseases at the same time. Results are available in less than five hours — fast enough to allow the analysis of thousands of samples per day.

The TruSentry diagnostic system can also be deployed in a single national reference lab, processing millions of samples per year or as part of a larger network of separate satellite facilities that are at, or closer to, the point where samples are collected. Other configurations can be deployed remotely in the field, for example, at the point of an infectious disease outbreak.

At the heart of the TruSentry system is nanoscale biosensor technology on three dimensional gel-drops licensed from Argonne National Laboratory in Illinois. Known as a biochip, this high-throughput form resembles a 96-well microtiter plate but in a 1 centimeter by 1 centimeter area that contains several dozen to several hundred "dots" or small drops. These biochips also are available in a microscope slide-size format for use in point of care settings. Each serves as a miniature laboratory with a unique protein, antibody or nucleic acid that will attach to a particular DNA sequence or antigen to identify infectious diseases such as TB, multidrug-resistant TB, HIV, viral hepatitis B, hepatitis C, syphilis and influenza.

"What Akonni has been able to do with the innovations licensed from Argonne is a very fascinating success story," says Yash Vaishnav, Ph.D., M.B.A, senior manager, intellectual property development and commercialization, Division of Technology Development and Commercialization (TDC), at Argonne National Laboratory. "It illustrates what can happen when innovative technologies, developed by two international research facilities, with cultural and geopolitical differences, fit well together, and a technology transfer office and licensee work together to overcome challenges."

International Collaboration Leads to Biochip

The special nanoscale biosensor technology is the result of an international research collaboration originally started in 1988 by the late Professor Andrei Mirzabekov, Ph.D., and his team at the Engelhardt Institute of Molecular Biology in Moscow and subsequently advanced via a joint research agreement in 1995 with Argonne National Laboratory. Argonne is one of the U.S. Department of Energy's (DOE) oldest and largest national laboratories for science and engineering research.

> *One of the many inventors who worked on developing this innovative technology is Daniel Schabacker, Ph.D., team leader, Bio-Detection Technologies at Argonne, where he is the lead scientist for the development of the biochip portfolio. Schabacker helped develop the technology for manufacturing the biochips in a commercial setting.*

“When I joined the Argonne team, many aspects of manufacturing and scalability of biochips had not been worked out,” Schabacker says. “It was interesting, with a lot of capabilities, but there was no manufacturing mindset — the manufacturing process needed to be scalable to be commercially viable.

“We really developed a package of standard operating procedures and a cost analysis that showed how our biochips could be marketable and manufactured in a commercial environment. We also transitioned from the original gel-pad concept to gel drops, which increased efficiency and produced a robust product.”

Since this international group of researchers started collaborating in 1993, development of the biochip has been supported with $22 million in funding from government and private sponsors — U.S. National Institutes of Health, DOE, U.S. Department of Defense, U.S. National Institute of Allergy and Infectious Disease, Centers for Disease Control, Motorola Inc., and Packard Instrument Co.

The Argonne National Laboratory biochip point-of-care diagnostic portfolio contains 29 issued U.S. patents with six pending applications, and the Argonne TDC has granted three exclusive licenses with defined fields of use to:

- Safeguard Biosystems — focusing on veterinary diagnostics
- Aurora Photonics — developing biochip imager for research and diagnostics
- Akonni Biosystems — developing human diagnostics

Innovations Licensed to Startup

Akonni first approached the Argonne TDC in 2003 after hearing Mirzabekov talk about detecting TB in human samples. As a startup biotech company, Akonni wanted to license the strong portfolio of intellectual property relating to this innovative microarray technology to raise funds.

After submitting a business plan and completing a licensing questionnaire, Argonne worked with Akonni to identify key patents and exercise an option agreement to negotiate a license prior to the request for seed funding. After the funding was obtained, they entered into license negotiations.

Argonne’s Vaishnav says the first exclusive license included biochips for TB and a few other infectious diseases, a reasonable upfront fee and royalty rates, and due diligences based on sales and commercialization activity. As the relationship matured, it became clear to both that they needed a more dynamic agreement beyond standard licensing. The result was a collaborative research approach with the guidelines that allowed for advancing the technology and developing prototype applications of the biochip.

Over the years, many of them filled with time-consuming processes and difficult challenges, Vaishnav says both parties took a flexible approach that resulted in the agreements to evolve so they could overcome risks, attract more investors and collaborators, and take advantage of growth opportunities.

Today, the relationship is guided by a fine-tuned license that includes an equity stake for Argonne in Akonni and a cooperative research and development agreement. The result is a successful relationship: So successful, in fact, that former Argonne staff, including a key biochip researcher, have joined Akonni, and both entities are working constructively with others to bring the technology to the marketplace.

“This technology adds a molecular diagnostic solution where the current technology, while good, simply can’t perform,” says Kevin Banks, vice president of sales and marketing at Akonni Biosystems. Unlike today’s real-time PCR-based platforms, the Akonni TruSentry system, Banks says, can rapidly screen a sample for hundreds of disease markers at

one time by using hundreds of molecular biosensors in a microarray the size of a fingernail thanks to all the work, not only at Argonne and Akonni, but the original research started by Mirzabekov and his team.

Akonni, which is deploying the technology in both point-of-care and high throughput screening settings, is in the process of attaining U.S. Food and Drug Administration approval for its diagnostic tests. Banks says this is a major milestone on the road to clinical trials and eventual clearance to market it as a commercially available diagnostic system.

“At the end of the day, what we have developed together is a third-generation molecular diagnostic solution that can provide truly accurate and trusted results, combined with alert detection and reporting on the world’s most prevalent and dangerous infectious diseases,” Banks says. “It represents the future of molecular diagnostics — a rapid, cost effective diagnostic system can greatly help immigration and health care officials identify and slow the spread of potentially dangerous diseases and would benefit all people.”

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