UCSF Researchers Win $900K NIH Grant to Create Array-Based Portable Pathogen-Detection System

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Researchers at the University of California in San Francisco will use an $888,000 grant from the National Institutes of Health to develop a rapid, pan-viral microarray diagnostic for category A-C biodefense pathogens.

Led by Charles Chiu, the director of the UCSF-Abbott Viral Diagnostics and Discovery Center, the team hopes the one-year grant will help them develop a quick, affordable assay that will be deployed in public-health laboratories for disease surveillance.

Chiu told *BioArray News* last week that his lab will co-develop the assay with Frederick, Md.-based Akonni Biosystems, while the UCSF Clinical Microbiology Laboratory under the direction of Steve Miller and Jean Patterson's lab at the Southwest Foundation for Biomedical Research in San Antonio, Texas, will validate it.

The test is based on the Virochip, a pan-viral, 20,000-probe microarray that covers 1,800 viruses and was developed by Chiu's fellow UCSF researchers Joe DeRisi and Don Ganem (*BAN 7/3/2007*). The aim of Chiu's project, funded in part through the American Recovery and Reinvestment Act of 2009, is to condense the Virochip to a "portable, smaller format with a rapid turnaround time that can be selective for detecting biothreat agents," he said.

Chiu said that the current version of the Virochip is manufactured by Agilent Technologies, costs between $150 and $200 per sample, and has a turnaround time of between 12 and 24 hours. Chiu's goal is to convert that to an assay with a turnaround time of fewer than two hours that can be purchased for between $10 and $15 and can be performed on a portable Akonni instrument.

Chiu said that he plans to request additional funding in coming years from the NIH to support the project.

"The plan is [to take] over five years to do the validation and to deploy the instrument out to collaborators in large public health agencies, at the point of care, to institute a surveillance system for the next potential outbreak or pandemic," Chiu said.

Founded in 2003, Akonni has developed and launched for research purposes a menu of TruArrays designed to detect tuberculosis, herpes, methicillin-resistant *Staphylococcus aureus*, and other indications. The firm claims on its website that the assays can be processed using its portable, benchtop instruments, in between 15 minutes and three hours, depending on the application.

Kevin Banks, Akonni's vice president of sales and marketing, told *BioArray News* this week that the company's TruDx2000 platform is being used in Chiu's project. Though Akonni has developed its own pathogen-detection TruArray assay, Banks said the assay Akonni is developing with Chiu's team is "much more comprehensive than Akonni's current product" and is "based on a different detection scheme."

According to Banks, the two products "are complementary with one another, not competitive." He said Akonni's category A-C TruArray has "more application for screening, whereas the genotyping array we're developing with Dr. Chiu will provide broader coverage and more detail about the pathogen."

Banks added that Akonni is providing the technology at a discounted price for the project. "We are providing technical insight pro bono, and we are working with Dr. Chiu to streamline the assay for product development," he said.

Chiu said that his team will be "piggybacking" on the platform that Akonni has developed. A main challenge for the project will be converting the content and protocol of the Virochip for use with Akonni's technology.

"They use 30-mer probes while we use 70-mer probes, and we will need to adapt protocols from Virochip to work on their platform," Chiu said. "But we know how Virochip behaves and know these probes will work in principle on the Akonni platform."

Chiu will also have to select the best probes for the new detection system. Current-generation Akonni arrays used with the TruDx2000 contain 500 probes, a technological limitation that moved Chiu's team to solely focus on US Centers for Disease Control and Prevention category A to C biothreat viruses, such as viral hemorrhagic fevers, including Ebola and Marburg, and arenaviruses such as Lassa and Machupo.

Other targets will include viral encephalitis, including Venezuelan equine encephalitis, eastern equine encephalitis, western equine encephalitis, and emerging infectious diseases such as Nipah virus and hantavirus. A complete list of the CDC's bioterrorism agents and diseases is available here.

"These are considered agents that have extreme pandemic potential or those that have high potential of causing mortality," said Chiu. "The NIH is concerned with those viruses that can cause severe pandemics."

A menu of 750 Virochip probes has already been selected as those most likely to detect each of the targeted virus families. Chiu said that his team will not target non-viral pathogens such as *Bacillus anthracis*, the bacterium that causes Anthrax.

The grant date for the project began Aug. 9 and will expire July 31, 2011. Chiu said that his main goal for the next year is to generate enough data to support future applications for funding. By the end of the first year, Chiu said he intends to have completed designing the array, with "careful selection of the best probes of Virochip for detection of these viruses as well as de novo probes."

Chiu will work together with Patterson's lab at SFBR to validate the probes on different pathogens. While Chiu's lab and the Clinical Microbiology Laboratory at UCSF are authorized to work with most pathogenic viruses, some, such as Ebola and Marburg, can only be processed at a higher security lab, such as Patterson's.

"We will have access to cultured samples, samples from inoculated primates or rodents, and we'll also be looking at positive samples from Africa of patients who have been infected with Lassa fever virus," Chiu said of the validation procedure.

Chiu also aims to know the initial specifications of the Akonni test, including its sensitivity, specificity, and limit of detection, by the middle of 2011. "I anticipate that all optimization steps will be done by next year and we will have Virochip probes working on the Akonni platform using their protocol," he said.

Looking forward, Chiu hopes in the future to deploy the system for use by collaborators in North America, Africa, and Asia, for the purposes of surveillance. He said that his lab has already recruited collaborators in Canada, Mexico, and India.

Finally, Chiu aims to place the assay under the purview of large public health agencies. "This will be added to typical assays for surveillance of influenza-like illnesses," he predicted. "They will be using it for surveillance of respiratory and diarrheal outbreaks and African participants will be paying special attention to hemorrhagic fever outbreaks."

By that time, Chiu also aims that the assay will be streamlined for regular use. "My vision is that this assay would be usable for someone without any array expertise," said Chiu. "This will be an easy-to-use assay that will be implemented on a push-button instrument."

'A Lot of Hurdles'

Pathogen detection is an area of interest for a number of researchers using array technologies, as well as commercial organizations. Influenza-detection assays, in particular, have been developed for surveillance use by firms such as Irvine, Calif.-based CombiMatrix; Potomac Falls, Va.-based TessArae; Sunnyvale, Calif.-based Arrayit; and Boulder, Colo.-based InDevr.

Beyond the US, firms like Singapore's Veredus Laboratories and Hyderabad, India's Ociumum Biosolutions have also developed flu tests.

None of these tests has received approval for clinical use in the US, though last year, the US Food and Drug Administration awarded TessArae an emergency use authorization to sell its Affymetrix-manufactured 2009 H1N1 influenza A virus assay, called the Resequencing Influenza A Microarray Detection Panel. The authorization expired on April 26, 2010, though it may be renewed (*BAN 12/22/2009*).

In addition to being used solely for research purposes, most array-based pathogen-detection assays are not as widely used as RT-PCR-based assays. "Effectively, these assays have to compete with RT-PCR," said Chiu of the array-based tests. "But there are a lot of hurdles.

"The biggest hurdle is that these assays have a long turnaround time and they are complex. The more probes you have, the more issues with clinical trials that enable you to get FDA clearance, so it's hard to get these arrays used routinely for clinical diagnostics purposes," he added.

Another reason array-based pathogen-detection assays have not been adopted en masse is that it is "hard to do the assays," said Chiu. Finally, cost hinders adoption of array-based assays.

"There is not enough volume for manufacturers to really lower their costs," Chiu said. "This is why the Akonni platform looked promising to us. From the outset they were able to print these arrays for $5."

Chiu said that dealing with cost and ease of use are the "major goals" of his current project. "It's a matter of decreasing cost, decreasing turnaround time, and making assays simpler," he said. "That's when you will see more broad adoption of these technologies."