University of Washington Launches Service Supporting Viral Diagnostic Tests

May 30, 2019 | Madeleine Johnson

NEW YORK (GenomeWeb) – The University of Washington has launched the Center for Viral Excellence, a service that can help companies and labs to evaluate diagnostic tests for viruses. The center anticipates that formalizing the service, and its expertise in sequencing- and droplet-based technologies, might differentiate it from similar services performed in other virology labs.

The center debuted with a booth and industry workshop at the Clinical Virology Symposium earlier this month. It was established in part by Alex Greninger, who is assistant director of the UW Medicine Clinical Virology Laboratory.

The target customers for the center are primarily diagnostics manufacturers, but the customers can also include manufacturers of viral standards, Greninger said in an interview.

For approximately 20 years, virology labs basically created their own laboratory-developed tests for clinical testing. But that has changed rapidly in the past five years or so, Greninger said, with a push toward automated, sample-to-answer testing. "Virology is becoming more like a chemistry lab," he said.

The transformation is not complete, and probably will never be, but there is still a lot of work that needs to be done to bring a growing number of new innovations to market. For example, companies frequently ask external labs to run validation studies and comparisons with gold standards and products that have already been cleared, Greninger said.

The services offered by the UW center include assay development and head-to-head assay comparison, which can be driven in part by the US Food and Administration's 510(k) process requiring comparison to an already-cleared test.

The center can also perform instrument and reagent evaluation and validation, contract clinical trial lab services, and economic modeling. In addition, the center offers access to clinical samples and sample banks, and experience with technologies that some companies may not have as much expertise with, like next-generation sequencing or digital PCR.

There are a handful of laboratory experts and virology labs that have come to the forefront as evaluators of tests and technologies. Experts such as Steve Young at TriCore Reference Laboratories, David Hilliard at ARUP Laboratories, Matthew Binnicker at Mayo Clinic, or Nathan Ledeboer at the Medical College of Wisconsin, are frequent co-authors of assay and instrument evaluations and comparisons.

"Everyone is doing this, we're just making it a little more formal," Greninger said.

Time is the most valuable commodity to companies trying to get tests to market, he also said, so having additional expert labs that can evaluate tests might be beneficial to the diagnostics space in general.

An example of the kind of virology work that needs to be done might be the evaluations that went into the Cepheid GeneXpert Ebola tests that are currently being run in the Democratic Republic of Congo, where there is an outbreak of the disease. These needed to be proved to work in the lab, as well as in the field, and evaluated for analytical sensitivity and specificity. This work was done by the manufacturer, but also through collaboration with clinical labs, Greninger said.

These collaborations are particularly useful to industry because clinical labs have various types of equipment, as well as access to the patient samples required to evaluate tests, and unique expertise. And for labs, these evaluations can be a source of revenue and can also give them early access to new technologies, perhaps to carry out studies they themselves are interested in.

"It helps get a little money on the side and allows them to use their expertise to scale technologies that they themselves would not be able to scale," Greninger said.

Equipment downtime is also an issue for large clinical labs, and a potential opportunity for lab revenue. For labs with sequencing and digital PCR systems, the amount of testing per week might be not as vast as that for standard qPCR systems, and these instruments tend to sit idle more often.

Greninger also said he believes the UW lab staff and others clinical labs that provide these services help companies with their unique understanding of clinical problems.

"A lot of smart engineers sitting in an office park can make really amazing tools," he said, but they aren't constantly bombarded with the questions and problems seen in clinical lab practice.

For example, he said the UW team has recently made some progress using digital PCR for HHV-6 diagnosis. In about 1 percent of people, HHV-6 virus has integrated into their genomes and can even be inherited in a Mendelian fashion, he explained.

"That means that 1 percent of the people that we test for HHV-6 are going to be rockingly positive with what looks like incredibly high viral loads, but there may not even be virus there," he said. Indeed, this phenomenon has recently caused some concerns for meningitis and encephalitis panels.

Another example of clinical virology expertise informing industry might be adenovirus diagnostics. There are a number of species of adenovirus. Serotypes 40 and 41, also called adenovirus species F, cause large outbreaks for which there is no treatment. Tests with primers specific to F adenoviruses make sense because that is the most important cause generally, Greninger said, but labs don't typically test people for adenovirus unless they are stem cell transplant patients, and in that case all 57 serotypes of human adenovirus are in play.

Greninger did his M.D. and Ph.D. work at University of California, San Francisco and did research with Joe DeRisi and a postdoc in the lab of Charles Chiu. His expertise in sequencing and metagenomics is complemented by the expertise of others in the UW virology department, such as Keith Jerome, David Koelle, and Linda Cook, who are all considered leaders in the field.

The center also expects that it will be able to connect people to an ecosystem of research expertise at UW, which could be helpful. For example, protein scientists, like David Baker or

Stanley Fields, could be helpful in the cases like the serological cross-reactivity among flaviviruses that has bedeviled tests for Zika and dengue.

"These are applied basic science problems for diagnostics, and we can connect [companies] to smart biochemists and computer scientists," Greninger said.

The center is now set up with 1,200 square feet of designated space, but it also uses some of the clinical lab space. Pricing for the different services will depend on the problem at hand, Greninger said. Linda Cook will be a full-time top-level member of the center; she is a special expert on international standards and virus quantitation.

The center has no projects as of yet that have made it through the contract pipeline at UW, but another hypothetical use case might be a CE-marked random-access testing instrument and assay that needs limit of detection and linearity ranges determined for several hundred samples prior to submission to the FDA, Greninger said.

Although reimbursement has been a challenge in the industry lately, particularly for respiratory viral testing, Greninger suggested that is, in part, because the prevalence of different viruses as the causes of disease in the population is unknown, because there are no good diagnostic tests in regular use. "It's almost like a vicious cycle," he said, but having a diagnostic test can perhaps lead to increased awareness, which in turn can result in development of new effective treatments.