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By Madeleine Johnson

NEW YORK (GenomeWeb) – Using fever to screen for Ebola casts a wide net, while standard RT-PCR requires many hours and expert technicians. Now, Madison, Wisc.-based Lucigen is accelerating development of a one-hour molecular assay to amplify and detect Ebola virus in decentralized settings like airports and emergency rooms.

The firm is currently pursuing US Food and Drug Administration Emergency Use Authorization for its point-of-care rapid Ebola diagnostic. The test relies on isothermal PCR and does not require extensive biosafety containment.

It will be the first of its kind, Lucigen director of business development Hemanth Shenoi told *PCR Insider* in an email. "To the best of our knowledge, there are no FDA-cleared or approved rapid point-of-care tests for Ebola or other hemorrhagic fevers; it is a 'blue ocean' market segment," he said.

When attempting to diagnose Ebola, fever can be masked, self-report of possible exposures is unreliable, and Ebola antibody testing is only effective in later stages of the disease. On the other hand, "current Ebola virus tests typically use RT-PCR methodologies, are designed for use in a BSL-4 containment lab, use costly and complicated instrumentation, and provide results in days," Shenoi explained.

Lucigen's test uses OmniAmp, the firm's patented thermostable polymerase with innate reverse transcriptase activity. The ultimate device will be a lateral flow cartridge with a fully integrated detection system.

The sample collection operates like a squeeze bottle, Shenoi said, suctioning up about 50 microliters of finger stick blood into a lysis buffer. The sample is then heated, and a portion is transferred into a reaction tube containing lyophilized reagents.

Isothermic amplification and detection are carried out on an Amplifire platform made by Lucigen's partner, Alexandria, Minn.-based Douglas Scientific. That instrument is portable and has a touch screen interface.

"It is the ideal fit for a field-deployable Ebola test instrument because of its light weight, small size, and ability to run on a rechargeable battery," Shenoi said, adding, "We are in discussions with Douglas Scientific on how we will bring the complete solution to market through the FDA EUA process."

Importantly, Lucigen is also working with an outside lab that has BSL-4 capabilities to "determine the effectiveness of inactivation of Ebola virus during the initial steps of the workflow," said Shenoi.

In July, Lucigen entered phase II of a $1.7 million Small Business Innovation Research award for an assay to detect and distinguish three strains of viral hemorrhagic fever — Ebola, Lassa, and Marburg.

As reported in *PCR Insider*, at that time the company had developed the rapid sample prep method and showed its feasibility with spiked blood samples. It had also figured out the best way to dry the necessary reagents, and demonstrated that lyophilized OmniAmp could be stable for more than 120 days at temperatures as high as 37°C.

Now, the exploding public health crisis in West Africa has caused Lucigen to increase its efforts on Ebola virus test development, Shenoi said.

"We will continue work on achieving the agreed-on grant aims; however, we are adding resources to work on the Ebola test to accelerate moving it from its current research feasibility stage to a stage where we can submit for an FDA EUA," Shenoi explained.

To that end, the company has also ramped up discussions with unnamed outside parties to accelerate development and commercialization of the test.

It also entered into several new collaborations to allow access to clinical samples, Shenoi said, including one that will evaluate the prototype test kit with patient specimens in Sierra Leone. "We are very excited about this collaboration, as access to clinical samples is one of the major barriers to Ebola virus diagnostic test verification," he said.

Lucigen's discussions with the FDA have only just begun, and the EUA process can take time.

Three Ebola RT-PCR assays have already been granted EUA since the Ebola emergency was declared in August — one from the US Department of Defense, and two from the US Centers for Disease Control and Prevention.

Meanwhile, Roche, Cepheid, and BioMérieux's BioFire Diagnostics are also pursuing, or considering pursuing, EUA for Ebola assays on their platforms, all of which are real-time PCR-based instruments designed for use in a laboratory.

However, Lucigen's molecular diagnostic technology is unique in that it is point-of-care. If ultimately approved, it may also provide traction for other POC molecular diagnostic devices, most of which have failed to make the jump from bench to bedside.

Lucigen is also discussing the possibility of more funding via the existing SBIR which could help it to hire additional scientists, obtain additional equipment, and perform studies required for FDA EUA submission, Shenoi said. The company has also been contacted by government and non-government organizations aware of the funded research. "Almost all are asking how they could help accelerate development of the Ebola test so that it could be deployed to address the major global public health crisis."

If successful, Lucigen's test might satisfy the need for molecular screening expounded in a recent op-ed in *The New York Times*. In that article, Columbia University's Siddhartha Mukherjee advocated a pilot RT-PCR Ebola testing program as a way forward in determining whom to quarantine.

"Dr. Mukherjee is correct that current strategies to contain the entry and spread of Ebola in the US are deeply flawed," Shenoi said.

"We also agree that policy makers should consider testing appropriate incoming travelers with molecular diagnostic methods; however, we believe that a highly accurate, cost-effective point-of-care molecular diagnostic test is a better solution," Shenoi said.

"A point-of-care test improves patient triage by focusing limited quarantine resources on those who are truly infected, allowing healthcare workers to protect themselves and others by testing their own health and facilitating testing at borders and airports to inform decisions, to safely allow or restrict access to the US," Shenoi noted.

Advancing decentralized infectious disease testing using PCR-based methods has been a high hope in the industry since the H1N1 EUA in 2009, as covered in *PCR Insider*. But whether the current Ebola EUA will ultimately spur changes in medical technology and clinician practices, bringing molecular diagnostics like Lucigen's to the bedside, remains to be seen.

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