

German Team Develops Bacterial Pathogen Test on Prototype Qiagen Compact Analyzer

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NEW YORK (GenomeWeb) – A proof-of-principle study from a team of German researchers has shown that a microfluidic disc assay and centrifugal processing platform can enable rapid and portable diagnostics.

The microfluidic cartridge, referred to as LabDisk, was developed at Hahn-Schickard, a microsystems engineering firm based in Freiburg, Germany. The disc enables rapid and fully automated bacterial pathogen detection using centrifugally-operated microfluidics and nested PCR with integrated sample preparation, according to the study, published last week in *Lab on a Chip*.

Interestingly, researchers at Hahn-Schickard have also built the microfluidic to perform "geometric multiplexing," whereby the extracted nucleic acid sample is automatically split via centrifugal force into more than a dozen reaction microwells that are pre-loaded to amplify different targets.

In turn, the assay disc runs using a platform called the LabDisk player, a point-of-need device being developed at Qiagen's Lake Constance center. This site has a focus on "point-of-need detection technologies," and was acquired about four years ago by Qiagen, Merle Hanke, global product manager for point-of-need, told GenomeWeb in an interview.

Jozef Drexler, a member of the R&D team at LakeConstance, noted in the interview that the firm has been developing the LabDisk player since 2009 via a number of different collaborative projects.

Like Qiagen's Rotor-Gene line of thermal cycler platforms, the LabDisk player can heat and cool reagents, spin them, and includes a detection system. However, the player has "a more sophisticated drive that can do microfluidics on a disc [by] using centrifugal forces to also perform, for example, sample preparation," Drexler said, thus enabling "everything from sample to result in the one player."

More specifically, the device can spin at multiple speeds, allowing it to essentially apply different levels of centrifugal force. It can spin an assay disc clockwise or counter-clockwise, or shake the disc back and forth, depending on the testing requirements. "You can also play with pressure and temperature to do all kinds of exciting things with the liquid on the disc," Drexler said.

For the system reported in Lab on a Chip, development was a collaboration, with Hahn-Schickard making the discs and Qiagen Lake Constance making the players. "They know more about the microfluidics and we know more about devices and detection," Drexler explained.

Hanke added that Qiagen "cooperate[s] with different companies or institutes in order to make the detection of their assay technology happen."

Such was the case with the firm's ESEQuant tube scanner platform for isothermal amplification, for example, which was developed for malaria detection in collaboration with the US Centers for Disease Control and Prevention, Hanke said.

The current collaboration with Hahn-Schickard also required parallel development, so that the forces the player applied could be optimized to direct the microfluidic flow on the disc.

Meanwhile, the corresponding author on the study validating the disc, Gregor Czilwik, said Hahn-Schickard is in the process of scaling up the manufacturing of disposable LabDisks and will offer OEM manufacturing to its partners in the future. A spin-off company is also being considered, he said.

The Lab on a Chip study used the system to measure spiked-in bacteria in 200 microliters of serum. This small volume is typical of the LabDisk player system.

The study showed a sensitivity of 3 colony-forming units of *Staphylococcus warneri*, 200 cfu of *Streptococcus agalactiae*, 5 cfu of *Escherichia coli* and 2 cfu of *Haemophilus influenzae*. It also showed a "sample-to-result" turnaround time of 3 hours and 45 minutes.

Researchers at Hahn-Schickard have also tested clinical samples, confirming neonatal sepsis in blood serum from about 30 samples, and they are currently optimizing that process. The group also has preliminary results showing concordance with bacterial culture for a small set of five clinical urine samples, Czilwik said, and is now seeking funding to expand the clinical testing.

Hahn-Schickard also has assays in development for diagnosis of respiratory tract infections, febrile illness, quantification of botulinum neurotoxin, antibiotic-resistant bacteria, and C-reactive protein quantification, Czilwik said, adding that there are other projects being done as contract research that are confidential.

Czilwik expanded on comparisons in the study between the LabDisk platform and other commercially available systems.

Compared to Cepheid's GeneXpert and BioMérieux's FilmArray, for example, the lab disc may be easier to manufacture and be more scalable in mass production, which could reduce cost.

"A LabDisk consists of a micro-formed plastic part sealed with a flat sealing foil; this is easy to manufacture," Czilwik said.

However, it also uses standard PCR reagents, and can perform other steps and techniques as well.

"Sample preparation, multiplexing, and even different assay formats like nucleic acid testing, immunoassays or clinical chemistry, including reagent pre-storage, can be implemented on the platform," Czilwik said.

This is in contrast with another commercially available centrifugal PCR platform, the 3M Integrated Cyclor and related assays from Focus Diagnostics. "The Focus disc ... does not include sample preparation or geometric multiplexing and requires addition of several reagents," Czilwik noted.

He later clarified that the Direct Amplification Disk does not include sample preparation because it uses a special amplification technology that can deal with usual inhibitors present in clinical samples. This is an advantage, although it potentially limits the possibilities for concentrating DNA. The workflow of that platform includes initial loading of the amplification mix along with the sample, prior to the analysis, he said.

Hanke affirmed some of the differentiating features of the LabDisk, highlighting that the disc-based assays are not restricted to nucleic acid amplification. "It is suitable for different applications or technologies and you have more flexibility with respect to the clinical need," she said.

Disc developers might also optimize assay speed by using isothermal amplification, or they could build multiplex assays for syndromic testing, she suggested.

And a further advantage of the player itself is that it can theoretically run different assay discs that use separate techniques on the same platform.

The firm has previously been funded for a bio-threat detection project using the platform, as well as an assay called ResCheck for respiratory pathogens.

The LabDisk player is still considered a prototype, and Qiagen has no concrete timeline for launch. Hanke also said the firm has no definitive plans concerning regulatory approvals in the EU or the US, and, as the OEM partner, that aspect may be up to the assay development partners.

The point-of-care market is certainly expanding, but the multiplexing ability of the LabDisk player is suitable for different applications or technologies and has more flexibility with respect to the clinical need, Hanke asserted. This allows for "cost-efficient syndrome-based testing," which may ultimately allow the platform to be competitive in the space.

As cost is also a factor in point-of-care settings, and that is the market this device is targeted for, the firm has an upper limit in mind, but Hanke said it was still too early to quote a price for the platform.