PCR Platform from Dutch Firm MBS Claims 30 Cycles in Two Minutes

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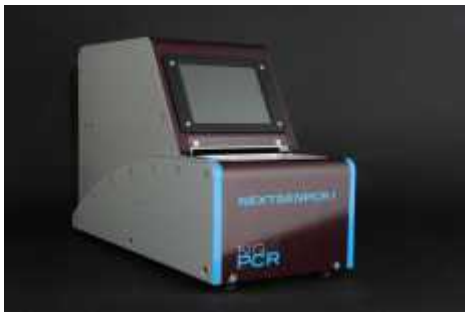
Premium



NEW YORK (GenomeWeb) – Dutch startup Molecular Biology Systems has developed a thermal cycler that boasts amplification times of less than 10 minutes for a standard oncology molecular diagnostic, and as little as two minutes for 30-cycle PCR assays. The firm announced this week that its platform, called NextGen PCR, has been adopted by Erasmus University Medical Center in the Netherlands for BRCA1 testing.

Founded in 2014, the firm received its first funding in April of 2015 and began development of the NextGen PCR thermal cycler one month later, founder Gert de Vos told GenomeWeb in an interview.

The system was developed by de Vos, a lab equipment inventor, after he began scrutinizing standard commercially available thermal cyclers. "It came from my head," de Vos said. "I invented it, tried it, and it worked the first time," he added. The firm has since applied for patents on the system.

NextGen PCR achieves 10 to 20 times faster thermal cycling than other commercially available technologies due to a number of innovations, de Vos said.

Firstly, the PCR reactions occur in very small microwells that are essentially indents in polypropylene foil.

Labs can use standard handling robots and automation systems to aliquot PCR reactions onto these wells, and the "plates" of foil sheets come in 96-well and 384-well sizes. The latter can hold 5-microliters of reaction volume per well, while the former comes in a 5- and a 30-microliters option. After reagents are aliquoted, a second sheet of foil is sealed on top, locking the reactions within the sheet.

The system takes these quilted polypropylene foil pouches, with their small pillows of PCR reaction, and compresses them between pre-heated blocks, mixing and almost instantaneously heating the small volumes, de Vos explained.

Then, spatial thermal cycling is applied, such that the sheets are shuttled back and forth, and compressed, between blocks heated to different temperatures for denaturation, annealing, and extension.

"We need five minutes in the morning to heat up the system, and then we keep the blocks at constant temperature and don't heat or cool any aluminum," de Vos said. Coupled with the faster reaction times, this reduces power consumption by up to 600 times per experiment, from 500 watts to 25 watts, according to the firm's website.

De Vos said the blocks are aluminum and of a mass that that reduces deviations in temperature down to 0.1 degrees Celsius. And because the plates are flat faced, the machine doesn't need to be reconfigured for different plate sizes.

The firm has also developed special foil-piercing pipette tips so that samples can be retrieved from the sealed wells.

Although he holds master's degrees from Leiden University in biology and physics, de Vos had to learn more about PCR and thermal cycling to attack the bottleneck of the speed of standard systems.

However, he noted that his inexperience may have helped him because he didn't rely on improving existing technologies. "I'm just a guy who doesn't know it cannot be done," he said.

Laboratorians at Erasmus were the first beta testers of the system. They presented research validating the thermal cycler for BRCA1 gene testing in a poster at the European Society for Human Genetics earlier this year.

In the poster, they reported less than 10-minute amplification of all 29 fragments of the BRCA1 gene using 29 primer pairs containing M13 tails for subsequent Sanger sequencing. The poster also noted separately that "a 100-basepair fragment could be amplified in less than 2 minutes," and that the cycler "allows for 10-20 times more reactions per cycler per day ... [and] reduces the number of instruments needed, reducing costs in purchase and maintenance contracts."

MBS is currently offering the NextGen PCR thermal cycler directly, but plans to build up a distributor network in Europe. So far, there have been several potential customers, de Vos said, although Erasmus is the first to adopt the system for testing. The firm plans to also expand sales to China, Japan, and the US as well.

The projected price for the system is €15,000 ($16,627), which is around twice that of some competing platforms. But although NextGen PCR may be pricier, de Vos believes the time savings the system offers will be a draw for customers. They will also be able to use many of the same consumables that are currently used, and the consumables the system does require are designed to be the same cost per plate as other commercially available platforms.

As for reagents, the system will accept whatever customers are currently using, for the most part. "It's a bit more limited, because obviously old-fashioned hot starts that take 15 to 30 minutes for initial denaturing don't make any sense all of a sudden," de Vos said.

MBS is now working on a qPCR version of the system using clear seals in collaboration with an undisclosed firm in Germany, de Vos said. It is also continuing its collaboration with Erasmus University and with the University of Groningen for microbiology research, and it plans to expand its academic collaborations as well.

The firm is also working on publications describing the technology, and anticipates the system will be particularly useful for time-critical diagnostics, such as prenatal or infectious disease testing.

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