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Miroculus Launches Digital Microfluidics Sample Prep System at AGBT, Explores New Applications

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Credit: Julia Karow Miro Canvas

MARCO ISLAND, Florida – San Francisco-based startup Miroculus this week unveiled its commercial digital microfluidics system for next-gen sequencing library preparation at the Advances in Genome Biology and Technology annual meeting, after showcasing a prototype of the instrument and early data at several conferences last year.

The system, called Miro Canvas, uses electrowetting technology to move droplets around in a cartridge and allows users to set up a series of reactions, such as NGS library prep protocols, in an automated and miniaturized way.

It mirrors other efforts to automate low- to medium-throughput NGS library prep, for example the Agilent Magnis NGS Prep or the Agilent Bravo, but with a microfluidics approach.

Miroculus is currently looking for customers for its beta program to test the system for whole-genome sequencing, exome sequencing, and RNA-seq library prep workflows. This will be followed by a full commercial launch later this year.

The system will have a list price of around $25,000 but the price of the one-time-use cartridges, which can each process a single sample, has not been determined yet.

During a company workshop at AGBT on Tuesday, Miroculus CSO Fay Christodoulou pointed out several features that set the Miro (formerly called Aeros) technology apart from previous sample prep systems that also relied on electrowetting.

The electrowetting approach acquired somewhat of a bad reputation from Illumina's Neoprep, a sample prep instrument that launched in 2015 and was discontinued just two years later, reportedly because of poor performance. Illumina originally obtained the electrowetting technology through its acquisition of Advanced Liquid Logic (ALL) in 2013. ALL had previously deployed the technology in another NGS sample prep device, called Mondrian SP+, that it developed for NuGen Technologies.

One important difference between these earlier systems and the Miro is that it doesn't immerse the droplets in oil but surrounds them with air. As a result, it can use more types of solvents and reagents, such as ethanol; it does not have problems with air bubbles; and samples can be retrieved without any carryover from oil. For reactions where evaporation needs to be prevented, which oil does effectively, the company has proprietary reagents available, Christodoulou said.

Another significant differentiator is that the Miro Canvas cartridges don't contain any electronics, which are all in the instrument and can undergo better quality control than a consumable.

The Miro benchtop platform opens up at the top to reveal an array of about 1,000 patterned electrodes that are coated with a hydrophobic insulator. Underneath are three thermal zones for heating, three magnetic zones, and one dual thermal-magnetic zone. A cartridge with two sides – one with standard microfluidic channels for actions like pipette-like mixing, the other side flat – is slotted into the instrument.

Using the Miro Palette software, customers can either choose a pre-programmed protocol or build their own protocol by combining the four main actions the system supports: washing, mixing, heating/cooling, and eluting. Essentially, users can "do everything you can do with pipettes on your bench," Christodoulou said. The system's software uses artificial intelligence to optimize the protocol, she said, and customers receive instructions for where on the cartridge to pipette their reagents.

Miroculus has tested the platform with three NGS library prep workflows, using kits from three different vendors, although it maintains that it can use any library prep reagents and is not restricted to specific kits.

Last year, in collaboration with researchers at the Broad Institute, the company demonstrated the use of the system for whole-genome sequencing PCR-free library prep, using the Kapa Hyper PCR-free kit and 200 ng of input genomic DNA, which took around 2.5 hours. The researchers showed that the Miro technology worked as well as the Broad's standard automated plate-based method and required less sequencing to achieve the goal of 20X coverage of 95 percent of the genome. Since then, Miroculus has reduced the input DNA to 50 ng while maintaining the coverage goal, Christodoulou said.

For exome library prep, a much more complex workflow, Miroculus has used the Twist Bioscience Human Core Exome Fast Hybridization with 50 ng genomic DNA, comparing it with a manual workflow. Libraries generated with the Miro technology showed equal or better complexity, target coverage, and uniformity compared to manually prepared libraries, according to the firm. Twist said on Tuesday that it is collaborating with Miroculus to bring its target enrichment and library prep kits to the Miro Canvas platform.

Finally, the firm has prepared RNA-seq libraries using the New England Biolabs NEBNext Ultra II directional RNA library prep kit and 1 ng to 50 ng of mRNA from liver and muscle samples. It found that for 50 ng mRNA, the most abundantly expressed genes were similar for manually prepared and the instrument-prepared libraries, and the two libraries had similar yields.

While it is preparing for the commercial launch of the Miro Canvas, Miroculus is already working on the next version of the instrument. The plan is to shrink the size and increase the density of the electrodes, to further reduce sample volumes, to increase the complexity of the workflows the system can handle, and to enable more samples to be processed in parallel.

Meanwhile, Miroculus and collaborators at the Stanford Genome Technology Center have been exploring other uses of the platform that go beyond NGS sample prep. On a poster presented at AGBT, they showed that they could enzymatically synthesize DNA on the instrument and then turn that DNA into a library for nanopore sequencing. As such, the instrument is able to encode information in DNA for storage and also decode it.

Christodoulou hinted at other future uses of the technology, for example to extract nucleic acids from biological samples, such as whole blood, plasma or saliva; to manipulate cells; or for cell electroporation.

In addition, the system could be used for combinatorial chemical synthesis. Last year, Miroculus and its collaborator GSK presented a poster, for instance, where they showed results from a feasibility study for carbon-nitrogen bond formation catalyzed by palladium. They concluded that the technology shows promise for a 'lab-on-a-chip' for the automated synthesis of compound libraries.

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