Cornell University Spinout Inso Biosciences Sees Opportunity in Long-Read Sequencing Sample Prep

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NEW YORK – Researchers from Cornell University, including Emeritus Professor Harold Craighead, a cofounder of Pacific Biosciences, have launched a startup to commercialize nucleic acid extraction and sample prep technology they developed and patented.

Inso Biosciences, currently based in Ithaca, New York, is targeting DNA extraction and sample preparation for long-read sequencing as its first application. But that's just one of the potential applications for the technology, licensed from Cornell, that uses physics, rather than chemistry, to grab DNA.

"We can complete sample processing in 30 to 40 minutes, not four to six hours," a tenfold decrease in time, said Inso CEO and Cofounder Harvey Tian. That's for DNA pieces 40 kb to 50 kb in length, he added, but they can be as long as 100 kb. Moreover, the firm's method keeps DNA in solution, which damages it less than chemical binding-based methods. Tian said the firm can successfully prepare samples for Illumina, PacBio, and Oxford Nanopore Technologies sequencers.

Inso is part of a "new wave of startups" in the sequencing sample prep market that are offering technical solutions to what has become a bottleneck for some researchers, said Julie Wolf, principal at 2048 Ventures, which led the firm's $2.2 million pre-seed financing round. "If you talk to the core [lab] directors, you'll see this is a hair-on-fire type of problem, even at academic level."

"High-molecular weight DNA extraction is a task that needs fine tuning and work," said Molly Zeller, lab manager at the University of Wisconsin Biotechnology Center DNA Sequencing Facility. "But once you figure out differences in sample types, the process can be quite smooth."

But for long-read sequencing to move toward the clinic, the field will have to find a way to reduce the time required for sample prep, Wolf said.

Inso's story began in Craighead's Cornell lab. After developing the semiconductor processing and photonics technology that underpins PacBio's single-molecule real-time long-read sequencing platform, he turned his attention upstream to technologies that he felt could enhance the emerging sequencing market.

A physicist by training who worked in the semiconductor industry before turning his attention to biology, Craighead said he pursued new mechanical methods of sample prep, rather than furthering development of chemical binding-based assays, such as magnetic beads.

The enabling technology for Inso is a microfluidic channel filled with an array of small pillars. It is akin to a plinko board, where the space between pillars gradually decreases the further into the channel the sample gets. These pillars obstruct biological material as it flows through and can catch cells or nuclei, while smaller objects — which can be collected and assayed as well — pass through. After lysis, the chromosomal DNA itself gets tangled on the pillars like spaghetti on a fork.

Tian, who was the last student to graduate from Craighead's lab, published his doctoral dissertation on the pillar array technology and was inspired to take an entrepreneurial route, both by the lab's history and the fear that this technology "would go into darkness" if he didn't try to commercialize it.

So far, the company is small, with only three employees — two of them full-time, including Tian — but he is looking to double that number by the end of the year.

Until recently, the firm had been funded primarily with grants. It won a $250,000 Small Business Innovation Research Phase I grant from the National Institutes of Health in 2021 to explore sample processing for tuberculosis diagnostics and a $225,000 SBIR Phase I grant from the National Science Foundation in 2020 to develop single-cell multiomic sample prep. Additionally, Inso recently completed an accelerator program with IndieBio, where Wolf first encountered the company.

"In general, we're a big fan of automation and solutions that free up scientists' time," she said.

Inso Bio is not alone in seeing opportunity in developing products that sit upstream of a sequencer. Volta Labs and Miroculus are two firms that have developed so-called electrowetting technology to automate and scale library preparation for NGS. They're backed by Illumina Cofounder John Stuelpnagel, 23andMe CEO Anne Wojcicki, and Kapa Biosystems Cofounder Paul McEwan and by Cota Capital and Section 32, respectively.

Technologies capturing the high-molecular weight DNA needed for long-read sequencing and optical mapping have already proved valuable. Last August, for example, PacBio acquired Circulomics for an undisclosed amount.

While Miroculus has already launched its platform and Volta Labs is expecting to do so later this year, Inso is still looking to build a marketable product. "Right now, we're in the phase of looking for new collaborators" and setting up pilot studies "to figure out what the customers want and what their pain points are before we finish our first product," Tian said.

Inso has four nonbinding letters of intent with potential customers and one pilot project with researchers at Cornell; however, the pilot is focused on size-based separation of cells and not long-read sequencing

sample prep.

Tian is targeting core facilities, clinical reference labs, and commercial R&D facilities as initial customers. "It's the people in charge of doing the sequencing, but who have the ability to make those purchasing decisions," he said.

Inso may also target the ag-bio sector. The firm's tech can remove secondary metabolites such as starch from "dirtier plant samples," Tian said, which make long-read sequencing harder.

In the near term, Inso wants to develop a compact, automated box that delivers long, high-quality DNA right to sequencers. "This is still a tabletop, research-level thing," Craighead said. "All of that has to be integrated and made more user-friendly; the goal is to have something as hands-off as possible."

Further down the road, the company could also look to provide sample prep for optical mapping, such as Bionano Genomics' Saphyr platform, or even for multiomics. The specifics of the technology allow for it to capture DNA, RNA, and proteins from the same cells, Tian said.

Ultimately, the firm hopes to seamlessly connect with sequencing platforms. Like Miroculus and Volta, Inso Bio's technology is based on microfluidics. Tian sees this as key to the future of sequencing. "What we see is that there are a lot of new kits or ways to do [sequencing sample prep], but not many are in a microfluidic format."

Moreover, "in the next few years, it's going to be harder and harder for short-read technologies to differentiate themselves well," he posited. "I think there's going to have to be more vertical integration to truly differentiate it, where a single system can take in samples, process them, sequence them, and analyze them on a closed system," he said. "We see ourselves as having that potential."

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