

IncellDx to Extend Precision Medicine Reach With Factorial Diagnostics Collaboration

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NEW YORK – IncellDx is extending its reach into the precision medicine space through its collaboration with startup Factorial Diagnostics by offering higher-resolution, multi-omic library prep kits for spatial profiling using its single-cell suspension platform.

The San Carlos-based firm is also developing a suite of COVID-19 diagnostic products that it believes will answer long-term treatment-based questions regarding patients still suffering from the disease.

Founded in 2010 by CEO Bruce Patterson, IncellDx has developed a two-step platform that performs single-cell molecular analysis without losing the intact cell. The company aimed to build a pre-analytical product package and analytical workflow that could accommodate any sample type.

The firm's sample prep technology uses a non-enzymatic approach for preparing single-cell suspensions from a patient's tumor. A technician starts by using a tissue punch to remove a portion of the tumor and then adds 800 ml of phosphate buffer saline to the sample. A small, non-shearing motor is added to the cuvette, and the device slowly homogenizes the tissue, releasing cells that can be analyzed in a single-cell detection system.

"We made it amenable for 20- to 30-color analysis, instead of using an embedded tumor tissue that, in the clinical sense, is less useful," Patterson said. The firm's single-use, micro-homogenizer, called IncellPrep, produces a usable sample within 5 to 10 minutes.

After sample prep, the second part of the workflow, called "simultaneous ultrasensitive signal-amplification hybridization in situ" (SUSHI), quantifies multiple proteins and molecular biomarkers inside the patient's isolated cells.

"The hallmark of the technology is to be able to prepare the cell for molecular biology without destroying it, yet in a way that it would be agnostic to the platform, whether using flow cytometry, imaging, and lately, CTCs," Patterson explained. IncellDx now offers a suite of library prep and diagnostic products using the two-step method for a variety of cancers, including bladder, lung, and breast cancer.

For example, the firm's HPV OncoTect 3Dx assay simultaneously detects and quantifies three molecular markers of cervical cancer: oncogene overexpression (E6/E7 mRNA), proliferation, and aneuploids in intact cells. The flow cytometry-based test analyzes 96 liquid-based Pap samples in less than four hours and helps clinicians identify which patients need to be further evaluated for the presence of high-grade cervical intraepithelial neoplasia.

Factorial Dx plans

As part of their agreement, IncellDx will offer Factorial Dx its IncellMax-Seq reagent to engage in in situ library preparation for next-generation sequencing (NGS) applications. The reagent, which keeps the

sample stable up to two weeks, maximizes different parameters such as cell yield and recovery before target cells are lysed and sequenced.

Patterson noted that Factorial Dx has unique library prep elements that complement IncellDx's approach. IncellDx also seeks to establish a presence in the sequencing space by developing a novel library prep workflow while keeping the platform affordable for customers.

IncellDx's ultimate goal for the project with Factorial Dx is to develop library prep kits that customers can run on their own sequencing instruments.

Patterson argued that traditional bulk, NGS cancer diagnostics can miss important phenotypic data during standard library prep, which typically involves grinding up the cells for their genomic components.

"While sequencing is great for yes and no answers and the reason we have licensed our in situ library prep technology to Factorial Dx ... our core strength remains in preserving the context of where the cell came from, such as what's in the cell and what its cell cycle looks like," Patterson explained in an email. With sequencing, "You lose all of the spatial relationships, which is critical, [because] in one breath you're talking about tumor heterogeneity, and in another breath, you're grinding whole tumor up."

This "spatial biology" market that IncellDx will enter with the collaboration already has tough competition from firms like 10x Genomics and NanoString Technologies. However, Patterson argues that the IncellDx's tech stands out because it can analyze "hundreds of thousands of cells" from a tumor not fixed in formaldehyde.

"In addition, we can look at the whole tumor, not just one slide of a tumor block," Patterson said. "Lastly, we can do mRNA, protein, and true cell cycle [analysis] all in a single high-throughput assay."

IncellDx's library prep platform labels the cell for "unequivocal identification," which is followed by isolating the cells based on immunophenotypic markers and lysing for downstream sequencing. Patterson highlighted that the method avoids analysis of doublets and allows "us to slap any number of identification markers, or even diagnostic markers," on the cells during the library prep portion of the workflow.

"We don't want to be in the instrument business as part of our business model, but instead want to realize [more than] 90 percent margins in reagent kits, making them agnostic to platforms around the world," Patterson said. "Much like ArcherDx, where they sell high margin kits, we want the end user to have some flexibility in its utility."

IncellDx initially raised \$3 million in a Series A funding round in 2010, then performed strategic deals with BioReference Laboratories in 2012. Patterson said the firm has since lived on sales, as well as additional strategic deals with pharma and reference labs. The firm also holds a convertible note worth up to \$9 million, which it can use for purposes such as scaling manufacturing of its kits.

COVID-19 research

While expanding its reach into the precision medicine space with Factorial Dx, IncellDx is also shifting its attention toward diagnostic products to aid COVID-19 treatment. Rather than developing a rapid diagnostic assay, however, Patterson said that the team instead chose to think "four steps ahead" and

decide what would be the natural next step in terms of diagnostic capabilities, settling on diagnostics for therapeutic efficacy and patient management. The team hopes to offer its technology to help clinicians determine why "long-haulers" still feel ill and are symptomatic two to three months post-infection.

Specifically, IncellDx is about to launch a COVID-19 cytokine storm-specific kit, which Patterson said the firm will ultimately submit to the US Food and Drug Administration for Emergency Use Authorization.

IncellDx has identified CCR5 as an important target for COVID-19 and will push its assays to market as soon as possible. Patterson said the firm is ramping up efforts because it is aware of at least four companies developing therapeutics for the disease.

"We resisted the urge to go outside of our business model, [to] just follow the money, and come out with a COVID-19 rapid diagnostic or serology test," Patterson explained. "We will be able to address [four] questions: when do you treat, how much do you treat with, how long do you treat, and during post therapy ... is [the patient] back to where [they] should be? "

Even if the demand for COVID-19 research and development eventually drops over time, Patterson believes that IncellDx's research can apply to other infectious diseases that are associated with cytokine storms, such as seasonal influenza and respiratory syncytial virus.

IncellDx currently holds 53 issued patents related to its library prep technology — in addition to 35 number of filed patents for its suite of COVID-19 products — with the US Patent and Trademark Office and international patent agencies.