Newsbytes

How one research lab morphed into a COVID-19 testing lab

July—In the early days of the COVID-19 pandemic, when the University of California, Berkeley's Innovative Genomics Institute decided to rapidly shift gears from conducting research to testing the community for SARS-CoV-2, some insiders may have thought the university was biting off more than it could chew under a tight timeframe. Yet a look at the lab 23 days later surely had any doubters eating their words.

The research lab, led by executive director Jennifer Doudna, PhD, renowned for her pioneering CRISPR (clustered regularly interspaced short panlindromic repeats) research, had to not only put in place a new virus test, it had to create a Health Insurance Portability and Accountability Act-compliant laboratory information management system to manage patient testing records and conform to Clinical Laboratory Improvement Amendments regulations, requirements it did not have to adhere to when it operated in a research capacity. And all of this, and more, had to be done at breakneck speed on a campus that did not have a medical school or hospital.

Dr. Urnov

When the project began, on March 14, recalls Fyodor Urnov, PhD, the institute's scientific director for technology and translation, UC Berkeley's student health center had at least a week-long turnaround for student SARS-Cov-2 test results, and there was a dearth of rapid testing in Berkeley and surrounding communities, even for first responders.

"We could not have a month-long research and development effort and then a month-long period to set things up," says Dr. Urnov. "It was just not an option." Therefore, the institute purchased Third Wave Analytics' cloud-based Lockbox LIMS and, working with the vendor, customized it to accommodate the needs of its SARS-CoV-2 test. Within approximately three weeks, the system was up and running.

The LIMS "harvests the data automatically — what specimen was requisitioned, by whom, when it arrived, who processed it, on what robot, using what procedure, when, what happened, and what was the result," explains Dr. Urnov. "It does that in a seamless fashion." More specifically, the LIMS provides such functionality as the ability to create records of samples when sample barcodes are uploaded, as well as automated record updating during sample testing, according to correspondence in *Nature Biotechnology* detailing the process of setting up the new lab (Amen AM, et al., published online June 18, 2020). Among the LIMS' many other capabilities are customized dashboards for tracking samples throughout the testing process and automated analysis of control and sample data to generate a final patient result immediately after raw data are uploaded.

To meet specific user needs, the institute created two LIMS interfaces — one for the university and one for the community. To test UC Berkeley students, the team built a direct interface to the student health center's EHR system. When a physician affiliated with the health center orders a lab test through the EHR, a de-identified barcode is linked to the order and automatically routed to the LIMS. Once the test is completed, the LIMS returns the barcoded data to the EHR for placement in the patient's medical record.

This process is not suitable, however, for orders coming from outside the university's health care system, Dr. Urnov says. "Everybody else has their own EHR. Somebody has Epic, somebody has something else. So, we solved that once and for all by building our own physician portal." The secure HIPAA-compliant portal resides on the

Salesforce.com platform. Physicians with login credentials can use the portal to enter the required testing information, initiating a test order that will be managed by the LIMS from start to finish.

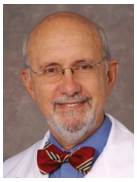
The necessity to move quickly also prompted the lab to adopt Thermo Fisher Scientific's TaqPath COVID-19 Multiplex RT-PCR diagnostic kit, Dr. Urnov says. While the institute's research scientists have extensive experience developing polymerase chain reaction-based tests, Dr. Urnov decided it would be faster to take a commercial test kit and adapt its workflow to suit the lab's needs.

To this end, the lab added automation to boost throughput, Dr. Urnov says. "Regular laboratory equipment is not set up to process 1,000 of anything. It's set up to process 10 of something. So we took the kit apart and we looked around for the best automation hardware — robots that could do hundreds and hundreds of samples without the 'error proneness' that humans are known for."

The new workflow involves using Hamilton's Microlab Vantage liquid-handling system in the RNA extraction phase, followed by Applied Biosystems' QuantStudio 6 Flex Real-Time PCR system to run the test, after which the LIMS software analyzes the test data, Dr. Urnov says. The combination of equipment greatly increased processing capacity, he adds. "The bottom line is, in a setting where 100 specimens take three hours, we now have a setup that will do 1,000 specimens in 12 hours."

The institute also made a workflow change to the test by using the virus inactivation solution DNA/RNA Shield, from Zymo Research, to protect staff handling patient specimens. When a health care provider obtains a specimen and puts the swab in a tube, DNA/RNA Shield inactivates the virus in a way that still allows the lab to measure nucleic acid levels, Dr. Urnov explains.

Because Thermo's equipment is being used in a manner that does not fall within its prescribed workflow and because of other workflow changes introduced by the lab, the test is classified as laboratory developed by the FDA and Centers for Medicare and Medicaid Services.



Dr. Green

With the adaptations came hiccups, says Ralph Green, MD, PhD, who is laboratory director for UC Berkeley University Health Services, as well as professor of pathology and laboratory medicine at UC Davis, outreach director for UC Davis Outreach, and lab director for UC Davis' student health laboratory. In one instance, says Dr. Green, difficulty finding the right tubes due to supply bottlenecks led the lab to purchase tubes that were shorter than the recommended size. The shorter size prevented the automated probes from reaching the optimal tube depth. As a workaround, says Dr. Green, someone in the laboratory turned to a 3D printer. "They used a 3D printer to produce a kind of mini-platform to put in the bottom of each of the 96 positions and then put the shorter tubes on top of those platforms. It worked."

In tandem with such efforts to transform the institute into a clinical lab that could serve the community, Dr. Green guided the team through the process of meeting FDA standards, state regulations, and CLIA requirements. This included filing paperwork with state regulators and CMS to extend the UC Berkeley student health center's CLIA certificate to the new clinical laboratory. It also involved obtaining necessary approvals to allow members of the institute's team to work in a CLIA lab.

As CLIA lab director, Dr. Green remotely oversees regulatory compliance issues for the lab and proficiency testing. He also reviews and validates test results, which may involve making decisions about the need to retest patients based on inconclusive results. The laboratory oversight is conducted through regular phone calls and Zoom

conferences, he says.

After the COVID-19 lab went live, UC Santa Cruz Molecular Diagnostic Lab approached Dr. Green, who also serves as lab director for the UC Santa Cruz Student Health Center, about playing a similar role in that lab's effort to establish a temporary SARS-Cov-2 testing site. Consequently, Dr. Green helped shepherd that lab through the necessary regulatory requirements.

Back at Berkeley, the Innovative Genomics Institute has partnered with multiple organizations in the vicinity, including community health centers, to offer free testing. It will stay the course, says Dr. Urnov, until COVID-19 testing is no longer needed in that area. — *Renee Caruthers*

Indica Labs collaborates on digital COVID-19 repository

The computational pathology software provider Indica Labs has partnered with Octo, an information technology systems provider to the federal government, to offer an online COVID digital pathology repository.

The repository provides a collection of high-resolution microscopic COVID-related human tissue images and is hosted at the National Institutes of Health. "COVID-DPR was created to enable international collaboration by providing a centralized, cloud-based repository for sharing and annotating digital whole slide images of lung, liver, kidney, and heart tissues from patients infected with COVID-19, as well as the closely related coronaviruses associated with SARs and MERs," according to a press release from the companies. The whole slide images, annotations, and metadata in the repository will serve as a reference data set for education, research, and clinical trials.

COVID-DPR is supported by Indica Labs' Halo Link software, a collaborative image-management platform designed to securely share digital whole slide images and data. When used with COVID-DPR, Halo Link software is deployed in a Web portal developed and managed by Octo and Axle Informatics to provide a secure, globally accessible central repository. Biomedical scientists can add, view, annotate, analyze, and share whole slide images using Halo Link. Indica Labs' image analysis, machine learning, and artificial intelligence tools can also be integrated and accessed in the software's interface.

The initial data sets in COVID-DPR were provided by infectious disease laboratories across North America, Europe, and Australia. The repository is available at https://covid19pathology.nih.gov.

Indica Labs, 505-492-0979

Voicebrook offering free Web-based reporting tool

Voicebrook has introduced Report Builder Lite, a free Web-based reporting tool that provides standardized grossing templates that can be used with any anatomic pathology system.

"It's not a replacement for our full-feature VoiceOver PRO software, but it's a stopgap for people needing an interim solution to help patients get results more accurately and more quickly," according to a company press release.

Report Builder Lite offers a variety of grossing templates for synoptic and narrative reporting. Once users assemble their structured reports, they can copy the text and insert it into an AP system. The product provides a library of the most common reporting templates, including those needed for emergency surgery.

Report Builder Lite does not save or transmit patient information via the Internet or interact with the user's AP system. To access it, go to www.reportbuilderlite.com.

Voicebrook, 516-326-9400

ONC and Sequoia Project extend interoperability initiative

The Office of the National Coordinator for Health Information Technology has committed approximately $1.1 million to continue for another year the Sequoia Project's role as the recognized coordinating entity to support

implementation of the Trusted Exchange Framework and Common Agreement. The TEFCA is intended to advance the secure exchange of electronic health information between health information networks.

In its role as the RCE, the Sequoia Project is charged with developing, implementing, and maintaining the TEFCA's Common Agreement and Qualified Health Information Network Technical Framework, which the ONC labeled a "single 'on-ramp' to nationwide connectivity."

"The TEFCA can help ensure that health information networks, health care providers, health plans, public health, and many more stakeholders have secure access to their electronic health information when and where it is needed most," said Michael Berry, an ONC subject matter expert, in an ONC Health IT Buzz blog post.

The funds will support the program for its second year, ending August 2021.

Novant Health partners with Zipline for drone deliveries

The Novant Health integrated health care system has announced that it is using drone deliveries to distribute personal protective equipment within its health system through a partnership with Zipline International, a provider of logistics services and drone flights.

"The operation provides contactless distribution of personal protective equipment and critical medical supplies to Novant Health frontline medical teams in the Charlotte, North Carolina, metro area," according to a press release from the company. Winston-Salem–based Novant has nearly 700 locations, including 15 hospitals and hundreds of outpatient facilities and physician clinics serving Virginia, North Carolina, South Carolina, and Georgia.

An emergency drone fulfillment center adjacent to the Novant Health logistics center in Kannapolis, NC, will launch the Zipline drones to distribute critical medical products to Novant Health hospitals. The operation is sending initial flights to Novant Health Huntersville Medical Center and will expand to other facilities in later phases.

In the early stages of the collaboration, Zipline will fly to Novant facilities in a range of 20 to 30 miles round trip. However, the Zipline drones can travel more than 100 miles, which would allow them to deliver medical supplies from the logistics center to more than 30 Novant Health facilities, with the necessary approvals.

The drones land only at the emergency drone fulfillment center. They make deliveries by hovering over a designated spot and dropping boxes of medical products fitted with paper parachutes. The drones can carry close to four pounds of cargo and fly up to 80 miles an hour, according to Zipline. They can also operate in severe weather.

The operation will provide drone flights in class D controlled airspace, where all air traffic is actively managed by the Federal Aviation Administration. The FAA approved the pandemic response operation under a part 107 waiver, which allows drones to fly in a manner otherwise prohibited by the agency's small unmanned aircraft regulations.

During the next two years, Zipline and Novant plan to expand their partnership beyond emergency operations to serve health care facilities, and perhaps patients at home, as part of a full commercial service, subject to FAA approvals.

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