360Dx

DiagMetrics Developing Capture Molecule- and Biosensor-Based Breath Assays

Aug 22, 2023 | Madeleine Johnson

Premium *Save for later*

NEW YORK – Startup DiagMetrics plans to parlay novel sample collection and detection technologies into home-use and point of care tests. The Madison, Connecticut-based company was recently awarded funding to develop easy-to-use mask-based COVID-19 assays for people with disabilities and intends to bring other infectious disease and critical care tests to the clinical and over-the-counter market.

John Daniels, an engineer, inventor, and registered US patent attorney who now serves as Diagmetric's CEO, said in an interview that the genesis of the firm came from his experience nursing his elderly parents through SARS-CoV-2 infections.

"They had both contracted COVID in their 90s, right at the beginning of the pandemic," he said.

With that, Daniels set about determined to develop a platform diagnostic that could be used at home and improve upon the low sensitivity of standard lateral flow immunoassays and high complexity of lab-based molecular testing.

In 2020, he, along with Ken DeCubellis, and Shekhar Wadekar, cofounded DiagMetrics.

DiagMetrics' first innovation was to use "an unused, unexplored biosample" called exhaled breath condensate, or EBC, Daniels said.

Nasal and oral swabs samples contain enzymes and contaminants that potentially impact test sensitivity, while traditional breath-based testing requires instrumentation to collect and detect volatile organic compounds, or VOCs.

But "warm vapor will always condense on a cool surface," Daniels said, generating an EBC sample that "is almost pure water" yet still contains bits of proteins that can potentially serve as biomarkers of disease. For EBC sample collection, the team has designed a face mask with a chilled microfluidic element that collects the breath's water vapor as it condenses.

The DiagMetrics team's second innovation was to use semiconductor biosensors rather than the traditional lateral flow elements with colorimetric or fluorescent readouts.

The team partnered with biosensor developers Sabine Szunerits and Rabah Boukherroub at the French National Center for Scientific Research in Lille, France, and, as described in an *Analytical and Bioanalytical Chemistry* study published last year, they initially deployed an electrochemical aptasensor approach to detect the S1 protein in breath.

But, a third innovation in Diagmetrics technology involves the use of detection molecules called nano clostridal antibody mimetic proteins, or nanoCLAMPs.

Developed by Kansas City, Missouri-based company Nectagen, nanoCLAMPs are small proteins that mimic antibodies. They are "engineered to be highly stable to proteases, high temperature, organic solvents, and alkali while exhibiting high affinity and specificity for their targets," according to Richard Suderman, Nectagen's cofounder and director of R&D.

Nectagen's customers typically use nanoCLAMPs to purify or identify a protein target of interest, Suderman said in an email, for example in the fields of bioprocess affinity chromatography, biosensing, and therapeutics. But the chemistry is amenable to diagnostics as well. In addition to DiagMetrics, Suderman said Nectagen recently collaborated with scientists at Queensland University of Technology in Australia to develop nanoCLAMPs as a component of an electrochemical biosensor to monitor methotrexate levels.

DiagMetrics' Daniels said that the nanoCLAMPs can be coated onto a semiconductor biosensor, and due to their smalls size, they can potentially interact with the binding sites on proteins, thus giving them "very good selectivity and sensitivity."

Once the nanoCLAMPs grab onto a target molecule, a slight change in the electron mobility of this capture molecule is detected by a field effect transistor (FET), a technology that also has the advantage of being self-amplifying, Daniels noted.

The current version of the DiagMetrics COVID-19 test can detect the virus in EBC in approximately five minutes. Testing starts once the required volume of condensate is collected, however, so in cases where a person is breathing more lightly the test time can be up to 10 minutes.

RADx Tech and beyond

Earlier this monthy DiagMetrics was awarded $938,784 in Phase I funding from the National Institute of Biomedical Imaging and Bioengineering (NIBIB) RADx Tech program, which is currently supporting the development of accessible over-the-counter COVID-19 tests.

With RADx's support, the firm plans to develop a mask-based COVID-19 diagnostic that incorporates Bluetooth connectivity to a phone app, enabling test instructions and results to be broadcast aloud to the user.

With the DiagMetrics test, users put on a mask and breathe, then get an audible result within minutes. This obviates the need to swab themselves, mix samples with reagents, and see the sometimes-faint lines of a typical colorimetric lateral flow test. The spoken instructions and results make the test amenable for use in children and people with physical disabilities as well, but Daniels said the ease of use could also make at-home testing simpler for everyone.

"You don't necessarily need to have low vision to be able to benefit from a simple device," he said.

At-home infectious disease diagnostics sales have proven to be tightly constrained by test price, but DiagMetrics expects its technology to cost in the $10 range. The biosensor is a common, small silicon wafer, Daniels said, and the Bluetooth connectivity element in the printed circuit board is also standard.

The assay currently uses a small button battery, he said, but the firm is looking into using near field communication instead. With such a method, the test is essentially powered by the cell phone antennae via standard technology used in radio frequency identification, or RFID tags.

"We're not developing a rocket ship," Daniels said, but rather "we're assembling existing components into a novel device."

The biosensors themselves can also be quickly functionalized through coating them with the appropriate nanoCLAMPs, so Daniels envisions being able to make assays for variant testing of rapidly evolving pathogens.

"We've got the capability to have the platform built and sitting on the shelf, and then when we know what the target is we can functionalize and have the devices deployed very quickly," Daniels said.

On the horizon for DiagMetrics are assays for other respiratory infectious diseases like influenza and respiratory syncytial virus, Daniels said, while bacterial infections like tuberculosis are also amenable to the EBC method.

The next iteration of the technology is expected to have six separate biosensors on a single chip in the biosensor, he said, to enable multiplexing and development of small panel assays. In addition, DiagMetrics is working to add VOC detection to its testing to further boost the multiplexing capabilities, and the firm is also honing the technology to potentially develop quantitative assays.

Beyond infectious diseases, the firm is looking into lung cancer detection and cardiac testing as potential spaces where EBC could be useful. For example, a prototype test detecting troponin in breath is "looking very good," Daniels said, adding that the Bluetooth capabilities could enable heart attack patients to be discharged sooner and have their troponin levels monitored from home in real time.

As part of its Phase I RADx milestones, the firm expects to show manufacturing scalability of a COVID-19 assay detecting the S and N proteins of the virus in the next six months.

The Phase II goals include scaling to a target of at least 150,000 units a month, Daniels said, at which point the cost of the test may also decrease. DiagMetrics is currently partnering with a foundry in Ithaca, New York to manufacture the biosensors but expects to work with an already-established manufacturing partner in India in the future.

Daniels added that the firm has carefully staked out the IP on the test methods and technologies. "Because it's a small company, the number one asset for us is the intellectual property," he said.

Filed Under + Point-of-Care Testing + Immunoassays + COVID-19 + Infectious Disease + Respiratory + North America + breath-based diagnostics + NIH funding