Clinical Research STRATEGIES

Development of Aptamer-based IVD and Digital App for SARS-CoV-2 Testing Under NIH RADx and NIBIB POCTRN Programs During Global Pandemic

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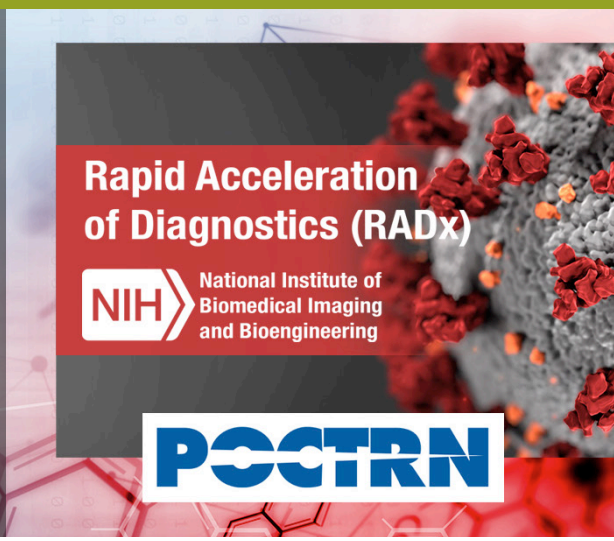

THE CHALLENGE

The challenge was to support a small three-person company with a myriad of regulatory, clinical, and business functions at a rapid pace under the NIH-funded RADx program. With aptamer-testing still a work-in-progress, the company had their work cut out for themselves to prove they could compete with other RNA-based testing.

Executive Summary

In April 2020, the National Institutes of Health (NIH) launched the Rapid Acceleration of Diagnostics (RADx) initiative with $1.5B in federal stimulus funding to speed innovation in the development, commercialization, and implementation of technologies for SARS-CoV-2 testing. Clinical Research Strategies (CRS) was invited to join the initiative as a US-based firm with strategic expertise in clinical, regulatory, and digital application development, and become a member of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) Point-of-Care Technologies Research Network (POCTRN). CRS was chosen by an early-stage biotech company to help drive multiple development milestones towards testing and validation of their saliva antigen test with biosensor and a digital app in preparation of point-of-care (POC) and over-the-counter (OTC) applications. This quick, affordable, aptamer-based biosensor has broad appeal to aid in the diagnosis of other diseases beyond SARS-CoV-2.

Background

Aptamers are functional oligonucleotides that can be designed to bind specific targets, akin to antibodies, but 100X cheaper to manufacture than antibodies. There are multi-fold benefits to utilizing the science of aptamers into diagnostics – new aptamer targets can be identified in under six days, manufacturing and scale-up, with chemical synthesis can occur in 24-48 hours with no batch-to-batch variation as seen with antibodies. An additional benefit of new diagnostic methods like aptamer-based platforms that are rapid, affordable, and sensitive, is that it doesn't draw from already overtaxed supply chains during a pandemic like COVID-19, and are necessary to meet the urgent need for POC and OTC testing.

The company's test resembles a standard Lateral Flow Immunoassay (LFA) and is designed to detect biomarkers from a 40µl sample of saliva in 15 min. This assay is coupled with a low-cost miniaturized potentiostat test strip for use as a COVID-19 POC or OTC diagnostic. Further, this disposable test will be supported by a fully fledged digital infrastructure for data collection, tracking, and tracing of COVID-19 test results via the company's mobile app.

First, high-affinity aptamers that bind to target viral proteins using a process known as direct aptamer-ELISA or ELASA were identified. Immobilization and density of aptamers on screen-printed gold electrodes to maximize the signal-to-noise ratio of the test was then optimized. The aptamers binding with high affinity to SARS-CoV-2 antigen were selected against the nucleocapsid (N) and/or spike (S) protein located on the surface of the SARS-CoV-2 virion. When the saliva

sample containing SARS-CoV-2 is loaded on to the test strip, the aptamers on the strip bind with high specificity to the SARS-CoV-2 surface proteins. The test strip is then inserted into the company's proprietary electrochemical test platform, where the virus-bound aptamers are detected via cyclic voltammetry, triggering a positive result. The result is sent wirelessly by the device to a mobile app via NFC (Near Field Communication), which facilitates unambiguous reporting, data collection, tracking, and contact tracing of COVID-19 cases.

The Ask

CRS was asked to develop clinical protocols, statistical plans, case report forms, informed consent forms, database, digital app roadmap and specifications, privacy programs, quality management system (QMS) and SOPs. CRS also conducted a literature review of aptamers for the development of an investors deck and key talking points. This program lasted nine months.

The Solution

Four members of CRS with expertise in regulatory sciences, clinical study development and execution, scientific and market research, digital know-how, and quality management system generation worked at the speed demanded by the project to provide multiple documents and presentations, and generate the knowledge base for the company towards continued success with their investor pitches and product development milestones.

THE OUTCOME

CRS supported the company in a variety of regulatory and background research asks for their investor pitch deck for the COVID-19 test, and to inform the expansion of their platform to other viruses/bacteria, as well as cancer diagnostics, etc., in future product development. An entire framework for the creation and data flow through the digital app was also outlined. Pathway to submission for Clinical Laboratory Improvement Amendments (CLIA) waiver by application, including dual pathways for 510(k) SE and CLIA Waiver, that could support the POC or over the counter indication for the saliva test was outlined. Extensive research was also done towards the world-wide current market availability of aptamer-based diagnostics and therapeutic products, as well as the pipeline of products in clinical trials, to provide evidence of viability of aptamers in multiple approved diagnostic and therapeutic products. A deep dive into current targets of aptamer-based detection tests utilizing Lateral flow Assays provided pathways to tweak the detection method of the LFA-based test if there arose a need to change from the company's current pathway of development. World Health Organization's "ASSURED" criteria for POC testing was investigated to help the company meet all the requirements and carry forth its vision of bringing a POC test to the underdeveloped countries around the world. This could help them target funding from foundations hoping to bring simple tests to rural population around the world.

Quotes

"Hugest thank you from the bottom of my heart personally, we got the top award for hardest working team at RADx."

— Chief Medical Officer

"Thanks to you and your team Alethea. I know (the company) really enjoyed working with you and the quality of your work was excellent."

— RADx-Tech Team Lead, RADx program

ABOUT THE AUTHOR

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Dr. Nisha brings 20+ years of research experience spanning both industry and academia, in clinical and regulatory affairs as well as basic and translational sciences. Dr. Nisha earned her PhD from Carnegie Mellon University in biological sciences and is a former NIH fellow whose scientific pursuits include genetics, epigenetics, molecular biology, immunology, and pre-clinical drug development research.

Dr. Nisha has facilitated FDA submissions for both drugs and devices, and, more recently, contributed to the updates of 100+ products under the new European Medical Device Regulation (EU MDR) requirements. Dr. Nisha has a rare blend of drug development and medical device expertise in all aspects of translational science, federal grants, clinical development and operations, scientific writing, regulatory affairs, and project management. Additionally, she has experience with multiple indications: respiratory and sleep, cardiovascular, ophthalmology, dermatology, metabolic disorders, pediatric immune disorders, precision medicine, regenerative medicine, and digital health. Dr. Nisha also remains actively involved with community outreach that fosters programs in STEM.

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