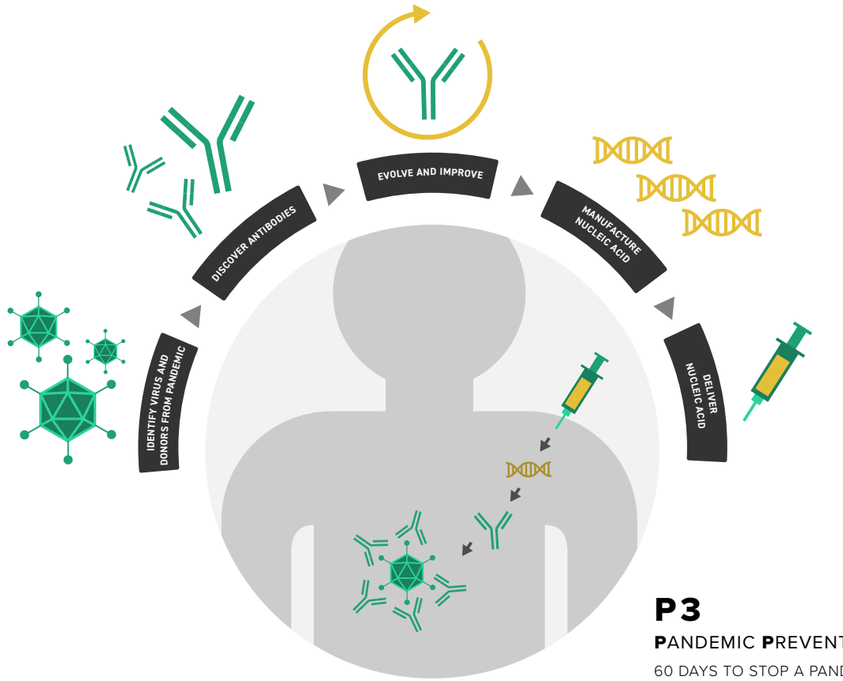
CASE STUDY

TWIST BIOSCIENCE

Speeding Up Antibody Discovery for Infectious Disease

Tasked with an ambitious goal from the Defense Advanced Research Projects Agency (DARPA) to develop a rapid response to help medical workers fight viral diseases in the field, Vanderbilt University Medical Center has already reduced the time to develop antibodies significantly. High-throughput, synthetic genes from Twist Bioscience have allowed the lab to expedite this process.

OCTOBER
2018



P3

PANDEMIC **P**REVENTION **P**LATFORM

60 DAYS TO STOP A PANDEMIC

Vanderbilt University Medical Center (VUMC) is recognized as a world leader in developing monoclonal antibodies for the treatment of infectious disease. The institution has isolated human monoclonal antibodies for many pathogenic viruses while pioneering the design of new antibody-based disease therapeutics and vaccines, many of which have progressed to clinical trials.

Because of this expertise, it was natural that the U.S. Defense Advanced Research Projects Agency (DARPA) would award VUMC a grant worth up to $28 million earlier this year. This funding allows the medical center to join a groundbreaking effort to develop new rapid response platforms for the discovery and delivery of antibodies to fight global viral threats like Zika and Ebola.

From Years to Weeks—Reducing Discovery Time

The ambitious project aims to significantly reduce the time and investment required to develop protective antibodies from lab to field — from years to just a few months.

The goal is for first responders and healthcare providers to have access to such treatments within 60 days of an outbreak of a viral disease, preventing escalation into a pandemic. Vanderbilt is one member of a team of institutions that are driving this effort, and who together will collectively push for such rapid responses. “Developing an integrated pipeline technology for identifying ultrapotent human antibodies and accomplishing rapid delivery … could revolutionize how antiviral interventions are conducted,” the DARPA agreement states.

A Race Against Time

Fighting what is essentially a race against time in speeding up the development of anti-viral antibodies, VUMC scientists enlisted Twist Bioscience in order to use its high-throughput platform to allow them to more quickly scale their antibody discovery process.

DARPA, through its Pandemic Protection Platform (P3) program, set the challenge to speed up the antibody identification pipeline to 60-days for infectious diseases. In a DARPA press release, Colonel Matthew Hepburn said, “P3 seeks to demonstrate an ability to rapidly produce virus needed to test and evaluate therapies, obtain high potency antibodies within the first weeks of an outbreak, and to scale delivery methods into humans to produce protective levels inside the patient.”

VUMC’s approach addresses these goals by vastly speeding up the antibody discovery, validation, and delivery processes. This accelerated process bypasses much of the cell-based work of their standard approach, and directly defines the genetic determinants of highly potent anti-viral antibodies directly from the serum of survivors. Numerous other innovations have also been coupled to this workflow to dramatically speed up the therapeutic candidate down-selection and selection processes.

Yet this process still took many months, or even years if it was a sufficiently complex challenge, Robert Carnahan, Associate Professor of Pediatrics at the Vaccine Center at VUMC, explained.

It’s expected that the lab will markedly improve its timeline for developing these therapeutics. “We had picked three different viruses and the last one will be unknown to us. They will give it to us and we’ll simulate a live event,” said James Crowe Jr., MD, director of the Vanderbilt Vaccine Center. “So it’s basically broken down into four sort of sprints, and we’ll try to get faster and faster. It’s kind of like athletic training.” VUMC’s agreement with DARPA states that the funding program will include four attempts over five years to successfully achieve the two-month response time.

Carnahan said the lab, using Twist Bioscience genes, has “discovered a way to markedly speed up the antibody discovery process.”

In a new approach to their human antibody screening, bioinformatics on the disease survivor’s B-cells separates out interesting antibody candidates. “From the pool of tens-of-thousands of antibodies in one patient, we can narrow it down bioinformatically to around 1,000 candidate sequences,” Carnahan explained. “We can then get synthetic genes for these candidates from Twist at an unprecedented speed and scale. We utilize these constructs in our recombinant antibody workflow to produce material for screening and selection in a matter of days. Combining the data from this screening process with our in-house bioinformatic analyses leads to identification of lead candidates, and helps us understand conserved characteristics of potent anti-viral antibodies.”

The current timelines for antibody development don’t fit into the requirements of the P3 platform. Access to large scale DNA synthesis is potentially going to allow the P3 platform to reach its 60-day goal.

CASE STUDY

Twist’s very high-throughput platform allowed us to quickly and efficiently examine thousands of possible antibodies in order to select the best results faster than ever before.

Robert Carnahan

ASSOCIATE PROFESSOR OF PEDIATRICS, VACCINE CENTER AT VUMC

A Complex Challenge

Importantly, VUMC’s approach is turning to pure synthetic biology, using recombinant systems to generate these important pharmaceuticals. By the very nature of their approach, synthetic DNA is essential to develop a process that worked as quickly and reliably as possible at a molecular level. VUMC chose to utilize synthetic DNA supplied by Twist Bioscience, as the company offers a highly scalable gene synthesis platform, where DNA is synthesised on silicon. High-throughput, affordable synthetic DNA from Twist Bioscience therefore allows researchers to accelerate the antibody identification process.

Accelerating the Antibody Identification Process

While VUMC researchers are still working to decrease the cost and time, while increasing the throughput of their accelerated antibody discovery process, Carnahan says they can see “the light at the end of the tunnel.”

“Twist Bioscience is the only provider that can scale to the quantities we need for this timeline,” Carnahan explained. “Twist’s very high-throughput platform allowed us to quickly and efficiently examine thousands of possible antibodies in order to select the best results faster than ever before.” ■

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