Lab developing a COVID-19 vaccine aimed at reaching billions

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Team members from the Love Lab (l-r) Neil Dalvie, chemical engineering; Andrew Biedermann, chemical engineering; Sergio Rodriguez, biological engineering; and Laura Crowell, chemical engineering. Credit: Massachusetts Institute of Technology

After cities shut down and citizens were urged to stay home to slow the spread of COVID-19, scientists in major cities like Boston were suddenly far removed from their labs. At MIT, on-campus research was

ramped down, reduced to only the most critical activities. That includes important work to better understand the virus and help stop the spread.

In the lab of Professor J. Christopher Love at MIT's Koch Institute for Iterative Cancer Research, a small team was cleared to return to the lab to continue their mission: generating and testing preclinical materials to push new vaccines for COVID-19 to reach the stage of conducting human trials on a much faster timeline than the many years that vaccine development typically takes. "It was like a blitz at the beginning to see if something would work," says Neil Dalvie, a graduate research assistant who's part of the Love Lab's onsite team, together with Andrew Biedermann, Laura Crowell, and Sergio Rodriguez, also graduate research assistants.

Everyone else from the lab coordinated from home, via Zoom, phone, and email. Dalvie says it's not the most efficient way to work. Having team members working remotely slows the whole process down, right when the need for speedy development has become most crucial. But the Love Lab got it done.

"We obtained preclinical material in a month," Dalvie says. Now, that material's ability to provoke an immune response is being tested in animal models with two lab partners to get to the next stage of development (a process that typically takes six weeks).

Timing matters, with the U.S. Centers for Disease Control and Prevention already reporting more than 45,000 U.S. COVID-related deaths. Researchers all over the world are working toward developing the first vaccines for COVID-19, but the Love Lab knows they can't just think about how fast they can make small amounts of the medicine, or how effective it will be at neutralizing the virus. The lab partners with the Gates Foundation, which has estimated that reducing the rate of infection worldwide will likely require billions of doses of COVID-19

vaccine. To reach that need, the Love Lab knows achieving such a goal will require thinking about manufacturing, too.

Currently, the U.S. Department of Health and Human Services is supporting Janssen Pharmaceuticals (a branch of Johnson & Johnson) in the development of 300 million vaccine doses, a fraction of the billions of doses that might be necessary. To address the gap, the Love Lab has thought constantly about how the solutions they are pursuing might scale in cost-effective ways. They have invoked a strategy they previously developed under a Grand Challenge for ultra-low cost vaccines to accelerate the readiness of preclinical materials for manufacturing as they advanced the first vaccine candidate toward animal and human trials.

"To reach the widest number of people, we need to be very intentional about incorporating in aspects of the manufacturability of a vaccine, even at the early stages of discovery," says Love, the Raymond A. and Helen E. St. Laurent Professor of Chemical Engineering. With this first vaccine candidate, his lab has furthered what they aim to be a new paradigm for vaccine development, by continuing to enhance the manufacturing process in parallel to the animal testing taking place. This approach could shorten the time required to transfer their processes to manufacturers who are simultaneously working to prepare to produce those materials in large quantities when ready. By overlapping these stages of development, the whole process becomes streamlined, as manufacturers learn to work with materials, becoming better-prepared to produce vaccines at the scale needed once trials are completed.

While this kind of platforming of the drug development process is common for the development of certain cancer drugs like monoclonal antibodies, Love says that's not the case for developing vaccines. "This is not a common approach in vaccine manufacturing," he says, explaining that normally, "Every vaccine is manufactured by its own unique

process."

For years, the Love Lab has sought to change this perspective, and now they're putting theories they've developed in the lab to the test in real-time. Crowell says more typically, a team would focus on showing they can validate a potential new drug, often just at small scales, before ever thinking about how to produce the drug on a larger scale. There was no time for that serial approach when it came to a COVID-19 vaccine. Manufacturing has had to factor into every development decision.

Rodriguez says the Love Lab's streamlining begins with applying knowledge gained from designing past processes and investigating how a given protein molecule could fit into an existing process. From there, the process is refined and enhanced, with simple tweaks to the sequence that improve the vaccine material's quality and manufacturability. For the current vaccine the Love Lab is testing, the team looked at the similar structure of the coronavirus SARS-CoV-1 as a starting point. "We can look at similar molecules to give us a ballpark or a benchmark for starting a production process to just try to find something that works for a first run," Rodriguez says.

They have also worked to improve production of the vaccine in parallel. "As we undertook our first production runs, we also developed faster methods to tailor our cell culture media formulation for COVID vaccine production to improve productivity and quality," Biedermann said. "We wanted to show that we can produce these vaccine candidates quickly and at concentrations relevant for commercial manufacturing."

What the Love Lab is developing is called a subunit vaccine, which works by using just a small part of a protein from the virus to train the immune system to recognize the whole virus and stop it from infecting cells. Such vaccines often work by invoking antibodies that can bind and neutralize the virus and give the body a fighting chance to destroy the

virus. Dalvie says the advantages of producing a subunit vaccine are that it's easy to make, safe, and, if the right protein is chosen "wisely," an appropriate protective immune response can be provoked.

The team's work has provided a fast solution to a first potential vaccine for further testing that also buys time while the team enhances the process and develops more robust vaccines that may produce a stronger immune response. Currently, immunogenicity and formulation studies are underway for the Love Lab's first vaccine candidate, but they continue to work on others. "This is a case where we may need multiple solutions to realize vaccines for many people," Love says.

Another aspect of manufacturing that the Love Lab considers is cost. It's important to produce an affordable vaccine if the expectation is for it to be widely dispersed, potentially inoculating two-thirds of the population. "Many of the vaccines in development now are likely going to be effective, but some of them may not be affordable in many parts of the world," Love says.

"A vaccine could be more broadly available at affordable costs—potentially all over the world," Dalvie says. "If we have also considered our ability to manufacture it."

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