BREAKING NEWS

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News > **Environment & Science** • News

Race for a vaccine: Synthetic COVID-19 viruses, built from scratch in the Bay Area, fuel critical research

Bay Area biotech labs craft custom-ordered genes for viruses and antibodies to speed up research

NEWARK, CA – FEBRUARY 20: Dr. Claes Gustafsson, co-founder of ATUM is photographed on Wednesday Feb. 20, 2019, in Newark, Calif. ATUM is a synthetic biology company that builds synthetic gene sequences of the COVID-19 virus. (Aric Crabb/Bay Area News Group)

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Even as most of us are hiding from the lethal COVID-19 virus, scientists need it to do research. But that can be dangerous and difficult.

So Bay Area labs are crafting the virus and its genes – synthetically and safely, tweaked so they're not infectious. Designed, built and shipped to labs around the world, these synthetic creations are accelerating the development of vaccines and drugs in ways that were impossible a decade ago.

"It allows us, as a society, to respond rapidly in a pandemic," said Claes Gustafsson, co-founder and chief commercial officer of ATUM, a Newark-based gene synthesis company.

"We can build things to specification," he said.

Constructed from scratch, like Legos, these products show the growing role of the burgeoning new field of synthetic biology, which builds living things from simple chemicals and nature's genetic blueprints.

In the last few years, this strategy has become faster, cheaper and more accessible. Genes, viruses, human antibodies and other components are as easy to order as an online purchase from Amazon.

The decades-old approach to vaccine development, for instance, is time-consuming and perilous. It requires growing vats of live virus. Samples of the virus must be shipped to vaccine-development laboratories. That creates delays and it may be considered too dangerous to transport the pathogen.

Then the lab must turn this deadly live virus into a safe variant, and propagate it in eggs or cultured cells.

That was the approach taken in early 2009, when the world was threatened by a pandemic strain of influenza called H1N1. A vaccine wasn't widely available until the outbreak was subsiding.

Similarly, the traditional search for immunotherapies — extracting protective antibodies from patients or producing them in animals — is hard, tedious, slow and difficult to scale to meet the massive need.

Synthetic biology enlists a very different strategy.

It's possible because of the Human Genome Project, which in 2003 gave us the ability to read nature's instruction manual, called the genome, like words in a book.

The virus's genetic instructions are encoded in 29,811 "letters" of RNA — the most irreducible unit of life, represented by the letters A (adenine), U (urasil), G (guanine) and C (cytosine).

The real opportunity, scientists say, lies in our ability to not merely read this new code, but to write it and then build something. Because each gene performs a predictable function, the synthesis companies are the scientific equivalent of a Kragen Auto Parts store.

Using off-the-shelf chemical ingredients – one chemical for each letter of the code – the genetic words are strung together. The companies can construct whatever a customer wants: One gene, a slew of genes or even a whole virus, almost identical but missing parts so it's not infectious. They also can build human genes to create protective antibodies and other proteins.

In the race to conduct COVID-19 research, it's all happened extraordinarily fast. In only three days after the virus was isolated from a mysteriously ill patient in Wuhan, Chinese scientists decoded its genome, then posted it online for the world to see.

Within hours of the code's posting, research labs from around the world sought to build it themselves.

By computer, they are sending their desired code to synthesis companies like ATUM, San Francisco's Twist Bioscience, San Diego's Codex or others.

Kristin Butcher, a research associate at Twist Bioscience in San Francisco, uses silicon engineering and chemical techniques to build genes from scratch. (John Green/Bay Area News Group)

Their goals vary. Maybe they're trying to find the viral gene that triggers the body's fierce immune response. That is critically important in designing a vaccine.

They may need the virus to screen the accuracy of new diagnostic tests.

Or perhaps they seek to construct lab-grown antibodies — critical for creating future immunotherapies. To identify which human antibodies are protective against COVID-19, scientists are writing many different variations of antibody gene sequences, ordering them, inserting them into mass-produced cells and then testing them against the virus.

"You have to try a billion potential antibodies to find the one that works," said Emily Leproust, CEO and founder of Twist Bioscience. Already, Twist scientists have identified dozens that bind to the virus, potentially neutralizing it, she said. Other labs are also racing to build antibodies.

When Stanford University needed proteins for their antibody tests, they turned to ATUM for large-scale, high-quality manufacturing.

All that's needed is a genetic code — and a credit card.

Customers range from universities and government labs to small biotech companies and large pharmaceutical corporations.

The gene companies say they screen customers and their orders to make sure that tomorrow's Hitler isn't ordering up the next smallpox, Ebola or yet-unnamed killer. Their software combs through the U.S. government's "watch lists" for terrorists and traffickers of weapons of mass destruction.

"We check every customer we send to," said Leproust. "We are fully aware of what people order."

Synthetic biology is not only shortening the design-build-test cycle of COVID-19 research, but also offers flexibility. Strategies can be tailored to match a viral strain that's circulating in a particular part of the world. Or they can shift if there's a sudden mutation in the virus.

Someday it might be possible to build products that protect us against all types of coronavirus, rather than just this specific one.

In a world where infections can travel as fast and far as a jet plane, synthetic biology makes it possible to build a biological defense at the speed of the internet.

"Because we can write DNA, we are able to develop diagnostic tests faster. And we are able to develop vaccines faster. We are able to develop antibody therapies faster," said Leproust. "It creates a massive acceleration of the timeline."

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