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## Will we be protected from COVID-19's omicron variant? Bay Area researchers sprint to find out

Little is known about the new variant, but local labs are gearing up to learn all about it



Dr. Catherine Blish, a globally recognized expert in infectious disease and immunology, is quickly designing studies to understand the behavior of the new COVID-19 variant Omicron at Stanford Medicine in Palo Alto, Calif. (Photo by Andrew Brodhead)

By [LISA M. KRIEGER](#) | [lkrieger@bayareanewsgroup.com](mailto:lkrieger@bayareanewsgroup.com) | Bay Area News Group

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Even before its arrival in the U.S., scientific labs in the Bay Area and around the nation are racing to build the experiments needed to answer two critical questions: Is omicron, which was first identified in South Africa, highly transmissible? Can it evade our immune response?

“We want to move quickly. We need to know more,” said Stanford University immunologist Dr. Catherine Blish, part of an informal consortium of experts from the Bay Area’s top research centers that was formed in expectation of the emergence of worrisome variants like omicron.

“We anticipated this would happen. This is what RNA viruses do,” she said. “And it was only a matter of time.”

Blish and other experts say there is no need to panic, because our vaccines will likely protect us from severe disease.

But the researchers are preparing for the worst. The new variant’s constellation of mutations — 32 on its spike protein compared to delta’s 18 — suggests it may spread more easily and dodge the immunity provided by vaccination or a prior infection.

Experiments at our region’s top labs — Stanford, UC San Francisco, UC Berkeley, the Gladstone Institute, the Innovative Genomics Institute and UC Davis — are joining the national effort to learn whether omicron can efficiently infect cells and whether our antibodies can fend it off. They will show whether current tests to detect the virus are still accurate and whether monoclonal antibody treatments still work.

Compared to our response to Delta, research into omicron is happening extraordinarily fast.

Delta arrived on the scene just as people were feeling a sense of hope that the pandemic might be fading, allowing a return to some sort of normalcy. But we let our guard down too quickly. Identified in India last December, it was first reported in the U.S. in March — when cases were already rapidly multiplying.

Omicron was detected less than a month ago, on Nov. 4 when a junior scientist with the South African Lancet Laboratories noticed a genetic anomaly in a single positive COVID-19 test. Similar findings were reported in Botswana. On Tuesday, a Dutch health agency reported that the variant had been identified in a test taken in the Netherlands on Nov. 19.

On Nov. 24, within two days of detecting a surge of cases, South African researchers analyzed samples from 100 infected patients and raised the alarm. The speed of the reaction is a testament to the country’s gene-sequencing capabilities.

Two days later, the World Health Organization classified it as “a variant of concern.” On Monday, WHO called an emergency meeting of an estimated 500 global scientists to accelerate efforts to understand the variant’s behavior.

While the U.S. has yet to identify any cases, the nation’s leading infectious disease expert Dr. Anthony Fauci has warned that it could already be here.

In the Bay Area and beyond, scientists have created an unofficial consortium — including Blish of Stanford, Dr. Melanie Ott of UCSF’s Gladstone Institute, Dr. Charles Chiu of UCSF, Dr. Sarah Stanley of UC Berkeley, Dr. Chris Miller at UC Davis, Dr. Michael Busch of Vitalant Research Center and Dr. Carl Hanson of the California Department of Public Health — that is working together to characterize new variants, such as omicron.

The collaboration of our regional labs means that some experiments can be coordinated, while others will be done in parallel, “giving us a lot more confidence in our results,” said Blish.

How, precisely, will omicron behave? To find out, labs need the virus — or parts of the virus.

Here’s the problem: The variant hasn’t yet been successfully grown by South African virologists. Once that’s achieved, it may be shared internationally. But its distribution could be stymied by trade restrictions.

Once the virus lands in the U.S., labs will quickly share the information, according to scientists.

Until then, Bay Area research labs are joining the global race to build it themselves. The goal is to create a “pseudovirus,” where some SARS-CoV-2 genes are inserted into a harmless virus. While it isn’t infectious, it behaves just like the real deal.

“Busy, busy,” said Claes Gustafsson, co-founder and chief commercial officer of ATUM, a synthetic biology company in Newark that constructs made-to-order synthetic proteins and genes requested by research labs.





NEWARK, CA – FEBRUARY 20: Dr. Claes Gustafsson, co-founder of ATUM looks over a rack of synthetic genes on Wednesday Feb. 20, 2019, in Newark, Calif. ATUM is a leader in a consortium of synthetic bio companies that screen orders of synthetic gene sequences to identify dangerous pathogens. (Aric Crabb/Bay Area News Group)

As news of omicron broke over Thanksgiving weekend, “I got hold of one of our key process guys while he was mountain biking far away and convinced him to find a desktop urgently to set up the order. We had someone else come in at 6 a.m. on his supposedly long lazy weekend to start the machinery,” Gustafsson said.

These synthesized pieces will also be used to tell us if the COVID-19 tests can detect the new variant. Twist Bioscience in San Francisco is designing so-called “controls” that reveal if a test is working correctly, said Twist’s Angela Biting.

“Every lab in the country that’s making these sort of viruses has contacted every (synthesis) company, hoping somebody can fill the order,” said Blish.

How quickly does the virus spread? How easily can it be transmitted? That’s one focus of the research effort.

Can omicron reinfect recovered people? How well does it evade vaccine-induced immunity? How vigorous a response is needed to knock it down? That’s the second major focus.

To find out, labs will challenge the variant with blood samples that contain different levels of protective immune cells, said UCSF infectious disease expert Dr. Peter Chin-Hong.

Blish’s lab at Stanford will focus on the body’s initial immune response to the variant, called innate immunity, which triggers neutrophils, macrophages and other cells to attack and kill. Her lab will also study how the virus infects and multiplies in so-called organoids, which are miniature noses and lungs.

At UCSF’s Gladstone Institute of Virology and Immunology, Dr. Melanie Ott plans on testing the entry, replication and infectivity of omicron in human cell and mouse models.

A team led by Dr. Charles Chiu of UC San Francisco will analyze the response of the new variant to antibody-rich plasma volunteered from 150 people have received the Pfizer, Moderna or Johnson & Johnson vaccine, as well as boosters. His research will also study the virus’s response to plasma from people who were infected by older COVID-19 variants.

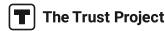
“The idea is to see: How do antibody levels wane, over time — and how well do they neutralize the new variant?” said Chiu. “If a patient has recovered from an alpha or delta infection, do their antibodies now neutralize omicron?”

The scientists think that people who recovered from COVID-19 or were vaccinated are unlikely to completely lose their ability to neutralize the virus. A booster dose will help build a stronger wall of defense.



"We're in a holding pattern for now," he said. "We're just waiting until there are cases identified in the U.S."

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### Lisa M. Krieger | Science/Research reporter

Lisa M. Krieger is a science writer at The Mercury News, covering research, scientific policy and environmental news from Stanford University, the University of California, NASA-Ames, U.S. Geological Survey and other Bay Area-based research facilities. She graduated from Duke University with a B.A. degree in biology. She splits her time between Palo Alto and Inverness, and in her spare time likes wildlife photography, swimming, skiing and backpacking.

[lkrieger@bayareanewsgroup.com](mailto:lkrieger@bayareanewsgroup.com)

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