Boston University researchers' testing of lab-made version of Covid virus draws government scrutiny

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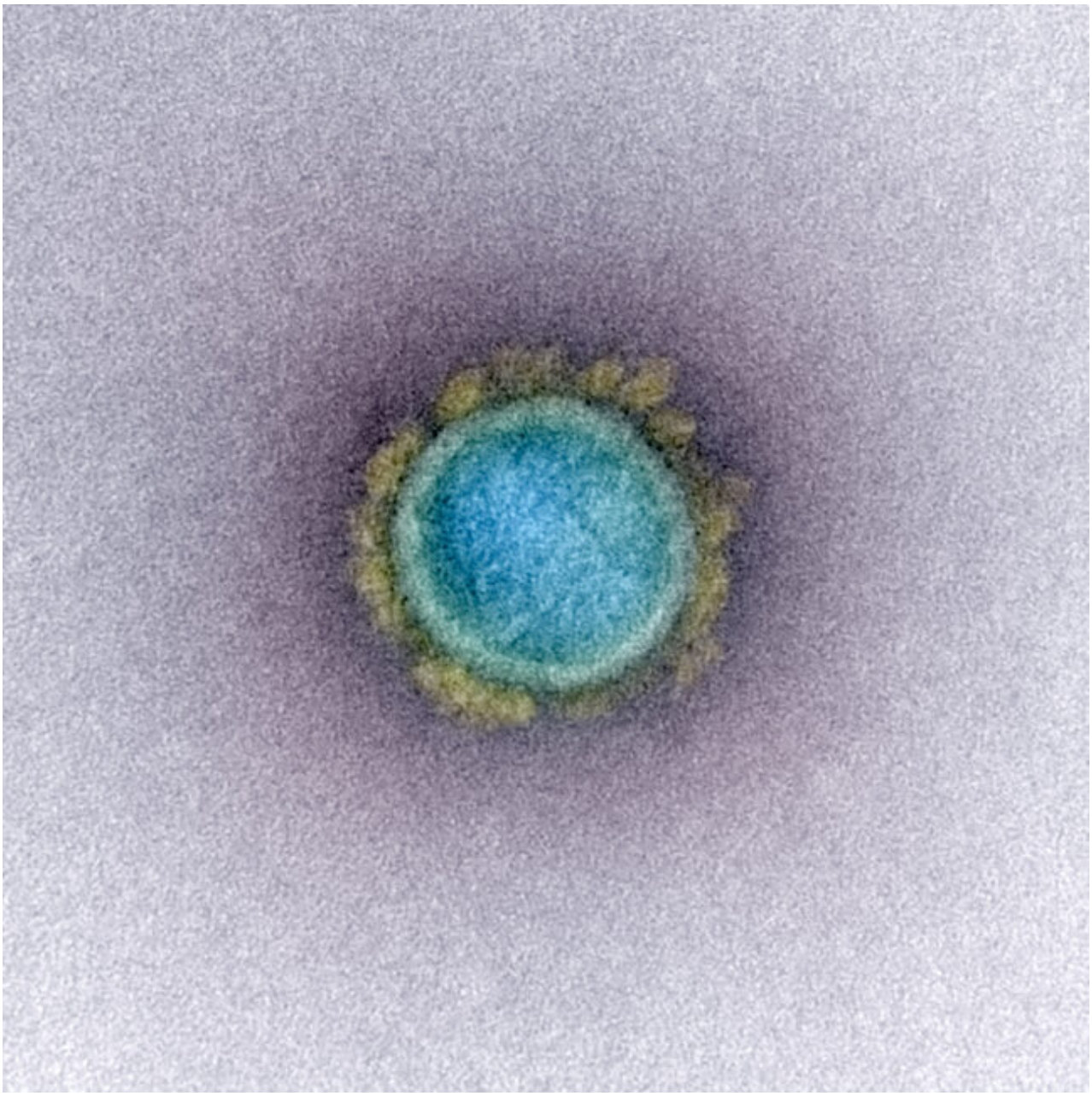

Research at Boston University that involved testing a lab-made hybrid version of the SARS-CoV-2 virus is garnering heated headlines alleging the scientists involved could have unleashed a new pathogen.

There is no evidence the work, performed under biosecurity level 3 precautions in BU's National Emerging Infectious Diseases Laboratories, was conducted improperly or unsafely. In fact, it was approved by an internal biosafety review committee and Boston's Public Health Commission, the university said Monday night.

But it has become apparent that the research team did not clear the work with the National Institute of Allergy and Infectious Diseases, which was one of the funders of the project. The agency indicated it is going to be looking for some answers as to why it first learned of the work through media reports.

Emily Erbelding, director of NIAID's division of microbiology and infectious diseases, said the BU team's original grant applications did not specify that the scientists wanted to do this precise work. Nor did the group make clear that it was doing experiments that might involve enhancing a pathogen of pandemic potential in the progress reports it provided to NIAID.

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"I think we're going to have conversations over upcoming days," Erbelding told STAT in an interview.

Asked if the research team should have informed NIAID of its intention to do the work, Erbelding said: "We wish that they would have, yes."

The research has been posted online as a preprint, meaning it has not yet been peer-reviewed. The senior author is Mohsan Saeed, from BU's National Emerging Infectious Diseases Laboratories. STAT reached out to Saeed on Monday but had not received a response by the time this article was published.

In emailed comments, the university later disputed the claims made by some media outlets that the work had created a more dangerous virus.

The email, from Rachel Lapal Cavallario, associate vice president for public relations and social media, said that the work was not, as claimed, gain of function research, a term that refers to manipulation of pathogens to make them more dangerous. "In fact, this research made the virus [replication] less dangerous," the email stated, adding that other research groups have conducted similar work.

In the paper Saeed and colleagues reported on research they conducted that involved creating a hybrid or chimeric virus — in which the spike protein of an Omicron version of SARS-2 was fused to a virus of the Wuhan strain, the original version that emerged from China in 2020. Omicron viruses first emerged in late 2021 and have since splintered into multiple different subvariants.

The goal of the research was to determine if the mutations in the Omicron spike protein were responsible for this variant's increased ability to evade the immunity to SARS-2 that humans have built up, and whether the changes led to Omicron's lower rate of severity.

The testing actually showed, though, that the chimeric virus was more lethal to a type of lab mice than Omicron itself, killing 80% of the mice infected. Importantly, the original Wuhan strain killed 100% of mice it was tested in.

The conclusion of the study is that mutations in the spike protein of the Omicron variant are responsible for the strain's ability to evade immunity people have built up via vaccination, infections, or both, but they are not responsible for the apparent decrease in severity of the Omicron viruses.

"Consistent with studies published by others, this work shows that it is not the spike protein that drives Omicron pathogenicity, but instead other viral proteins. Determination of those proteins will lead to better diagnostics and disease management strategies," Saeed said in a comment circulated by the university.

Research that has the potential to make pathogens more dangerous has been a hot-button issue for years. About a decade ago, a high-profile debate over whether it was safe to publish controversial studies done on a dangerous bird flu virus, H5N1, led to a re-writing of the rules around this type of work. Another review of the policy is currently underway, led by the National Science Advisory Board for Biosecurity.

The controversy around research on pathogens of pandemic potential has gained ground since the start of the Covid-19 pandemic, which some scientists and others believe may have been an accidental or deliberate result of research on bat coronaviruses at the Wuhan Institute of Virology in the Chinese city where the pandemic is believed to have begun. (There is a lot of evidence that points to the virus spreading from a wet market in the city, not the Wuhan lab. But proving something didn't happen three years after the fact is a challenge that may be impossible to meet.)

Under NIAID's policy, proposals to do federally funded research that could produce so-called enhanced pathogens of pandemic potential should be referred to a committee that would assess the risks and benefits of the work. The policy is known as P3CO framework.

Erbelding said NIAID would probably have convened such a committee in this case, had it known that Saeed's team planned to develop a chimeric virus.

"What we would have wanted to do is to talk about exactly what they wanted to do in advance, and if it met what the P3CO framework defines as enhanced pathogen of pandemic potential, ePPP, we could have put a package forward for review by the committee that's convened by HHS, the office of the assistant secretary for preparedness and response. That's what the framework lays out and that's what we would have done," she said.

Erbelding noted, however, that some of the media coverage of the study over-estimates the risk the work may have posed. “That 80% kill rate, that headline doesn’t tell the whole story,” she said. “Because Wuhan” — the original strain — “killed all the mice.”

The fatality rate seen in this strain of mice when they were infected with these viruses raises questions about how good a model they are for what happens when people are infected with SARS-2. The Wuhan strain killed less than 1% of people who were infected.

Virologist Angela Rasmussen, who was not involved in the research, had some sympathy for the BU scientists, saying there is ambiguity in the rules as they are currently written.

“Because so much of the definition of ePPP pertains to ‘reasonable anticipation’ of results in humans (and animal models are not always good proxies of this), it’s very difficult for researchers to say ‘Oh yes, this is ePPP,” Rasmussen wrote in response to questions from STAT.

“I’d personally reach out for clarification from NIAID when in doubt, but it’s often not obvious when additional guidance is warranted. And because it’s not very transparent, it’s hard to look at other decisions NIAID has made for examples,” she said.

“I’m very tired of people suggesting that virologists and NIAID are reckless or don’t care about biosafety,” said Rasmussen, a coronavirus expert at the University of Saskatchewan’s Vaccine and Infectious Disease Organization. “The problem isn’t that. The problem is that the guidelines and expectations aren’t clear for many experiments and the process isn’t transparent.”

— This article has been updated to include comment from Boston University and from the senior author of the paper.

About the Author Reprints

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