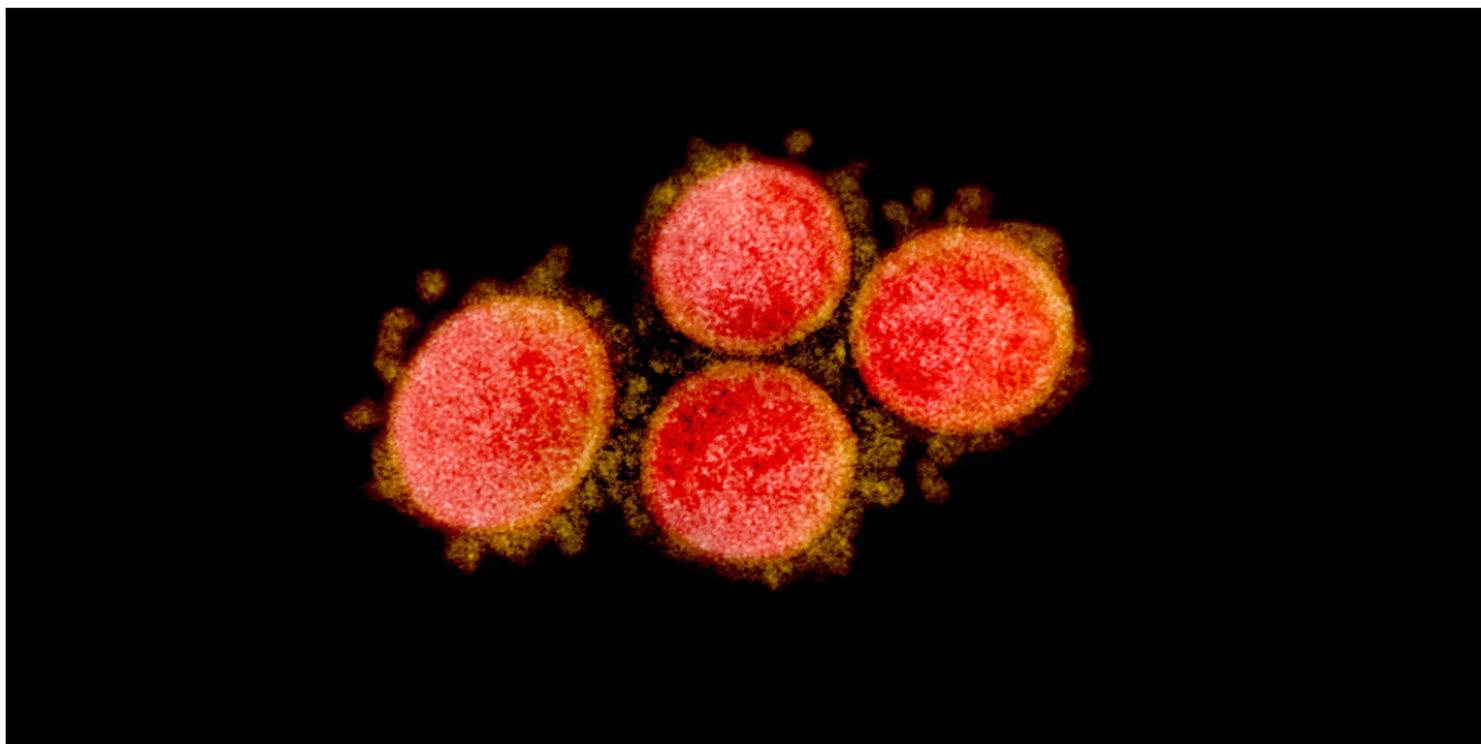


Sharon Lerner, Maia Hibbett

September 23 2021, 6:16 p.m.



Transmission electron micrograph of SARS-CoV-2 virus particles. Photo: Universal Images Group via Getty Images

A grant proposal [written by](#) the U.S.-based nonprofit the EcoHealth Alliance and submitted in 2018 to the Defense Advanced Research Projects Agency, or DARPA, provides evidence that the group was working – or at least planning to work – on several risky areas of research. Among the scientific tasks the group described in its proposal, which was rejected by DARPA, was the creation of full-length infectious clones of bat SARS-related coronaviruses and the insertion of a tiny part of the virus known as a “proteolytic cleavage site” into bat coronaviruses. Of particular interest was a type of cleavage site able to interact with furin, an enzyme expressed in human cells.

The EcoHealth Alliance did not respond to inquiries about the document, despite having answered previous queries from The Intercept about the group’s government-funded coronavirus research. The group’s president, Peter Daszak, acknowledged the public discussion of an unfunded EcoHealth proposal in a [tweet](#) on Saturday. He did not dispute its authenticity.

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Since the genetic code of the coronavirus that caused the pandemic was first sequenced, scientists have puzzled over the “furin cleavage site.” This strange feature on the spike protein of the virus had never been seen in SARS-related betacoronaviruses, the class to which SARS-CoV-2, the coronavirus that causes the respiratory illness Covid-19, belongs.

The furin cleavage site enables the virus to more efficiently bind to and release its genetic material into a human cell and is one of the reasons that the virus is so easily transmissible and harmful. But scientists are divided over how this particular site wound up in the virus, and the

cleavage site became a major focus of the heated debate over the origins of the pandemic.

Many who believe that the virus that caused the pandemic emerged from a laboratory have pointed out that it is unlikely that the particular sequence of amino acids that make up the furin cleavage site would have occurred naturally.

Adherents of the idea that SARS-CoV-2 emerged from a natural spillover from animal hosts have argued that it could have evolved naturally from an as-yet undiscovered virus. Further, they argued, scientists were unlikely to have engineered the feature.

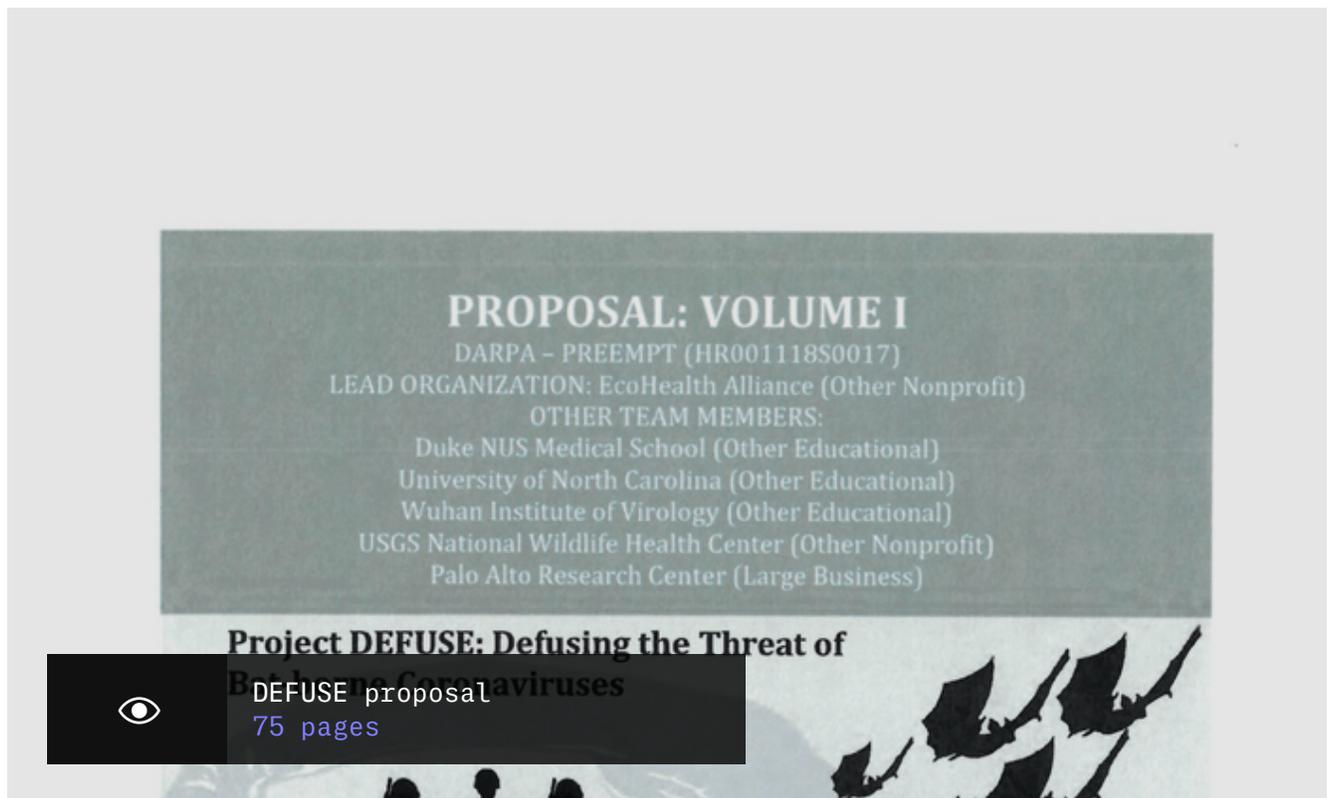
“There is no logical reason why an engineered virus would utilize such a suboptimal furin cleavage site, which would entail such an unusual and needlessly complex feat of genetic engineering,” 23 scientists wrote earlier this month in an [article](#) in the journal *Cell*. “There is no evidence of prior research at the [Wuhan Institute of Virology] involving the artificial insertion of complete furin cleavage sites into coronaviruses.”

But the proposal describes the process of looking for novel furin cleavage sites in bat coronaviruses the scientists had sampled and inserting them into the spikes of SARS-related viruses in the laboratory.

“We will introduce appropriate human-specific cleavage sites and evaluate growth potential in [a type of mammalian cell commonly used in microbiology] and HAE cultures,” referring to cells found in the lining of the human airway, the proposal states.

The new proposal, which also described a plan to mass vaccinate bats in caves, does not provide conclusive evidence that the virus that caused the pandemic emerged from a lab. And virus experts remain sharply divided over its origins. But several scientists who work with

coronaviruses told The Intercept that they felt that the proposal shifted the terrain of the debate.



Tipping the Scales

“Some kind of threshold has been crossed,” said Alina Chan, a Boston-based scientist and co-author of the upcoming book “Viral: The Search for the Origin of Covid-19.” Chan has been vocal about the need to thoroughly investigate the possibility that SARS-CoV-2 emerged from a lab while remaining open to both possible theories of its development. For Chan, the revelation from the proposal was the description of the insertion of a novel furin cleavage site into bat coronaviruses – something people previously speculated, but had no evidence, may have happened.

“Let’s look at the big picture: A novel SARS coronavirus emerges in Wuhan with a novel cleavage site in it. We now have evidence that, in early 2018, they had pitched inserting novel cleavage sites into novel

SARS-related viruses in their lab,” said Chan. “This definitely tips the scales for me. And I think it should do that for many other scientists too.”

Richard Ebright, a molecular biologist at Rutgers University who has espoused the possibility that SARS-CoV-2 may have originated in a lab, agreed. “The relevance of this is that SARS Cov-2, the pandemic virus, is the only virus in its entire genus of SARS-related coronaviruses that contains a fully functional cleavage site at the S1, S2 junction,” said Ebright, referring to the place where two subunits of the spike protein meet. “And here is a proposal from the beginning of 2018, proposing explicitly to engineer that sequence at that position in chimeric lab-generated coronaviruses.”

Martin Wikelski, a director at the Max Planck Institute of Animal Behavior in Germany, whose work tracking bats and other animals was referenced in the grant application without his knowledge, also said it made him more open to the idea that the pandemic may have its roots in a lab. “The information in the proposal certainly changes my thoughts about a possible origin of SARS-CoV-2,” Wikelski told The Intercept. “In fact, a possible transmission chain is now logically consistent – which it was not before I read the proposal.”

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But others insisted that the research posed little or no threat and pointed out that the proposal called for most of the genetic engineering work to be done in North Carolina rather than China. “Given that the work

wasn't funded and wasn't proposed to take place in Wuhan anyway it's hard to assess any bearing on the origin of SARS-CoV-2," Stephen Goldstein, a scientist who studies the evolution of viral genes at the University of Utah, and an author of the recent Cell article, wrote in an email to The Intercept.

Other scientists contacted by The Intercept noted that there is published evidence that the Wuhan Institute of Virology was already engaged in some of the genetic engineering work described in the proposal and that viruses designed in North Carolina could easily be used in China. "The mail is filled with little envelopes with plasmid dried on to filter paper that scientists routinely send each other," said Jack Nunberg, director of the Montana Biotechnology Center at the University of Montana.



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Vincent Racaniello, a professor of microbiology and immunology at Columbia University, was adamant that the proposal did not change his opinion that the pandemic was caused by a natural spillover from animals to humans. "There are zero data to support a lab origin 'notion,'" Racaniello wrote in an email. He said he believed that the research being proposed had the potential to fall in the category of gain-of-function research of concern, as did an experiment that was detailed in [another grant proposal](#) recently obtained by The Intercept. The government funds such research, in which scientists intentionally make viruses more pathogenic or transmissible in order to study them, only in a [narrow range of circumstances](#). And DARPA rejected the proposal at least in part because of concerns that it involved such research.

While Racaniello acknowledged that the research in the DARPA proposal entailed some danger, he said “the benefits far, far outweigh the risk.” He also said the fact that the viruses described in the proposal were not known pathogens mitigated the concern. “This is not SARS,” he said, referring to SARS-CoV-1, the virus that caused a 2003 outbreak. “It’s SARS-related.”

But SARS-CoV-2 is not a direct descendant of that virus – it’s a relative.

In fact, the viruses described in the grant proposal were not known pathogens. And the authors of the grant proposal make the case that because the scientists would be using SARS-related bat viruses, as opposed to the SARS virus that was known to infect humans, the research was exempt from “gain-of-function concerns.” But according to several scientists interviewed by The Intercept, the viruses presented a threat nevertheless.

“The work describes generating full-length bat SARS-related coronaviruses that are thought to pose a risk of human spillover. And that’s the type of work that people could plausibly postulate could have led to a lab-associated origin of SARS-CoV-2,” said Jesse Bloom, a professor at Fred Hutchinson Cancer Research Center and director of the Bloom Lab, which studies the evolution of viruses. Bloom pointed out that the scientists acknowledge the risk to humans in their proposal. “It’s an explicit goal of the grant to identify the bat SARS-related coronaviruses that they think pose the highest risk.”

Stuart Newman, a professor of cell biology who directs the developmental biology laboratory at New York Medical College, also said the fact that the viruses weren’t known to be dangerous didn’t preclude the possibility that they might become so. “That’s really disingenuous,” Newman said of the argument. “The people that are claiming natural emergence say that it begins with a bat virus that evolved to be compatible with humans. If you use that logic, then this virus could be a

threat because it could also make that transition.” Newman, a longtime critic of gain-of-function research and founder of the Council for Responsible Genetics, said that the proposal confirmed some of his worst fears. “This is not like slightly stepping over the line,” said Newman. “This is doing everything that people say is going to cause a pandemic if you do it.”



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While the grant proposal does not provide the smoking gun that SARS-CoV-2 escaped from a lab, for some scientists it adds to the evidence that it might have. “Whether that particular study did or didn’t [lead to the pandemic], it certainly could have,” said Nunberg, of Montana Biotechnology Center. “Once you make an unnatural virus, you’re basically setting it up in an unstable evolutionary place. The virus is going to undergo a whole bunch of changes to try and cope with its imperfections. So who knows what will come of it.” The risks of such research are profound and irreversible, he said. “You can’t call back the virus once you release it into the environment.”

DARPA, a division of the Department of Defense, said regulations prevented it from confirming that it had reviewed the proposal. “Since EcoHealth Alliance may or may not be the direct source of the material in question, and we are precluded by Federal Acquisition Regulations from divulging bidders or any associated proposal details, we recommend that you reach out to them to confirm the document’s authenticity,” a DARPA spokesperson wrote in an email to The Intercept. The British Daily Telegraph reported that it had confirmed the

document's legitimacy with a former member of the Trump administration.

The Telegraph story erroneously reported that the scientists proposed to inoculate bats with *live* viruses. In fact, they hoped to inoculate them with chimeric S proteins, which were proposed to be developed through a subcontract in the grant in Ralph Baric's lab at the University of North Carolina at Chapel Hill, not in Wuhan. Baric did not respond to The Intercept's request for comment.

Conflict of Interest

Many questions remain about the proposal, including whether any of the research described in it was completed. Even without the DARPA funding, there were many other potential ways to pay for the experiments. And scientists interviewed for this article agreed that often researchers do some of the science they describe in proposals before or after they submit them.

“This was a highly funded group of researchers that wouldn't let one rejection halt their work,” said Chan, the “Viral” author.

Perhaps the most troubling question about the proposal is why, within the small group of scientists who have been searching for information that could shed light on the origins of the pandemic, there has apparently been so little awareness of the planned work until now. Peter Daszak and Linfa Wang, two of the researchers who submitted the proposal, did not previously acknowledge it.

Daszak, the EcoHealth Alliance president, has actively sought to quash interest in the idea that the novel coronavirus originated in a lab. In February 2020, as the pandemic began to grip major cities in the U.S., he began organizing scientists to write an [open letter](#) that was

published in the Lancet addressing the origins of the virus. “The rapid, open, and transparent sharing of data on this outbreak is now being threatened by rumours and misinformation around its origins,” read the statement signed by Daszak and 26 co-authors. “We stand together to strongly condemn conspiracy theories suggesting that COVID-19 does not have a natural origin.”

Daszak directed and gathered signatures for the letter, all the while suggesting that he and his collaborators on the proposed DARPA project, Baric and Wang, distance themselves from the effort.

“I spoke with Linfa [Wang] last night about the statement we sent round. He thinks, and I agree with him, that you, me and him should not sign this statement, so it has some distance from us and therefore doesn’t work in a counterproductive way,” Daszak wrote to Baric in February 2020, just weeks before it appeared in the journal, according to an [email](#) surfaced a year later by public health investigative research group U.S. Right to Know. “We’ll then put it out in a way that doesn’t link it back to our collaboration so we maximize an independent voice.” Ultimately, Daszak did sign the letter.

“I also think this is a good decision,” Baric replied. “Otherwise it looks self-serving and we lose impact.”

Baric and Wang – a professor in the emerging infectious diseases program at Duke-NUS Medical School, Singapore – did not respond to inquiries from The Intercept about their decision not to sign the letter in the Lancet.

Daszak was also a member of the joint team the World Health Organization sent to China in February 2020 to investigate the origins of the pandemic, which concluded that it was “extremely unlikely” that the virus had been released from a laboratory. (In March, WHO [called](#) for

further investigation of the origins of the virus and stated that “all hypotheses remain open.”)

“I find it really disappointing that one of the members of the joint WHO-China team, which is essentially the group of scientists that were tasked as representatives of both the scientific community and the World Health Organization of investigating this, are actually on this proposal, knew that this line of research was at least under consideration, and didn’t mention it all,” said Bloom, of Fred Hutch. “Whatever information that relates to help people think about this just needs to be made transparently available and explained.”

Correction: September 24, 2021

A previous version of this article stated incorrectly that the EcoHealth Alliance proposal had been featured on Sky News Australia.

Correction: September 23, 2021, 3:30 p.m.

A previous version of this article stated incorrectly that Linfa Wang was a member of the WHO-China team.

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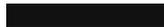
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