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Newly developed vaccine offers superior protection against omicron variants

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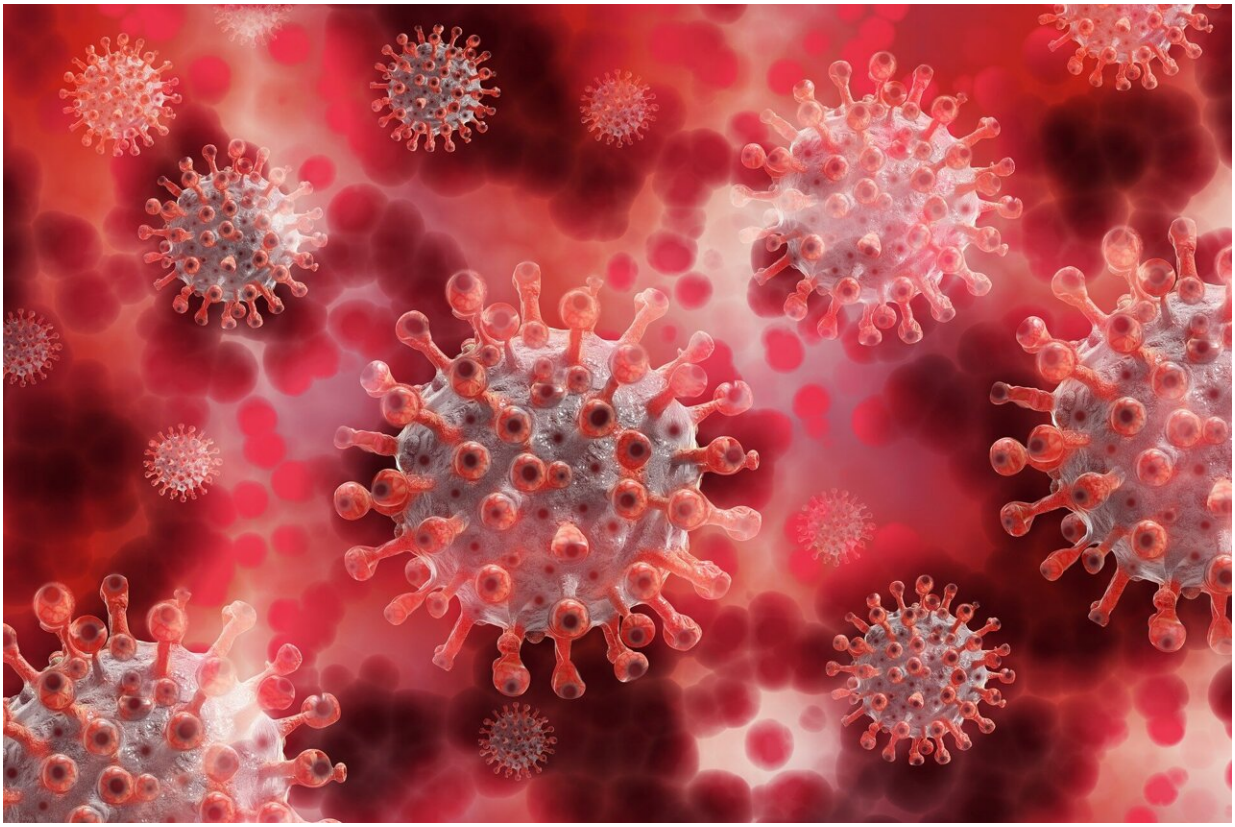

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Yale scientists have developed a novel omicron-specific mRNA vaccine that offers superior immune protection against two viral subvariants than standard mRNA vaccines.

The new vaccine, called Omnivax, increased neutralizing antibody response against the BA.1 and BA.2.12.1 omicron subvariants in pre-immunized mice 19-fold and eight-fold, respectively, compared with standard mRNA vaccines. The improved response against the BA.1 subvariant was reported June 6 in the journal *Nature Communications*. The results of the study involving the BA.2 subvariant were published July 19 in the journal *Cell Discovery*.

"While standard mRNA vaccines still offer protection against infection from new variants, their effectiveness wanes over time and was compromised due to immune escaping mutations in emerging variants," said Sidi Chen, associate professor of genetics at Yale School of Medicine and senior author of both studies. "We wanted to see if we could develop variant-specific vaccines that offer additional protection against emerging subvariants."

The experimental vaccines, developed in Chen's lab by a team headed by postdoctoral associate Zhenhao Fang, use engineered lipid nanoparticles to deliver mRNA to cells with "instructions" to create spike proteins from mutating variants, which the virus uses to attach to and infect cells. The presence of these foreign viral fragments prompts the immune system to create antibodies against the virus. The rapid mutation of spike proteins on the surface of the virus over time has created a parade of subvariants and enabled them to blunt the protection of earlier generations of mRNA vaccines developed by Moderna and Pfizer-BioNTech.

The engineered lipid nanoparticle mRNA vaccines can be created quickly, researchers say. For instance, the BA.1 subvariant emerged in mid-November; by mid-December Yale researchers had developed a vaccine against the new strain. However, testing the efficacy of the vaccine in mice and a peer review of the study was not completed until February. By March, the BA.2 subvariant had taken hold as the

predominately circulating strain throughout most of the world. The researchers then investigated whether the omicron variant vaccine maintains its superiority over standard vaccines against BA.2. The new vaccine has also boosted an immune response superior to standard vaccines in mice against this subvariant, researchers reported in the *Cell Discovery* paper.

"Although translating the new vaccine candidate from bench to bedside requires rigorous testing in human trials, these preclinical studies provide a comprehensive and unbiased evaluation of an omicron-specific vaccine candidate, which will hopefully fuel the development of next-generation COVID vaccines," Chen said.

In light of the rise of new BA.4 and BA.5 variants, which have become most common among COVID cases, Yale researchers are currently testing a new vaccine candidate against these variants in mice.

"We have a system in place to combat these emerging subvariants, but we need to adjust the system to respond more quickly to emerging health threats," Chen said.

Chen is affiliated with the Yale Cancer Center, the Yale Stem Cell Center, the Yale Center for Biomedical Data Science, and the Systems Biology Institute and Center for Cancer Systems Biology at Yale's West Campus.

Yale's Zhenhao Fang and Lei Peng are co-first authors of both papers. Chen is the corresponding author of both papers. Craig Wilen, assistant professor of laboratory medicine and immunobiology at Yale, is the co-corresponding author of *Nature Communications* paper.

More information: Zhenhao Fang et al, Heterotypic vaccination responses against SARS-CoV-2 Omicron BA.2, *Cell Discovery* (2022).

DOI: 10.1038/s41421-022-00435-w

Zhenhao Fang et al, Omicron-specific mRNA vaccination alone and as a heterologous booster against SARS-CoV-2, *Nature Communications* (2022). DOI: 10.1038/s41467-022-30878-4