Is a cheap 'universal' coronavirus vaccine on the way?

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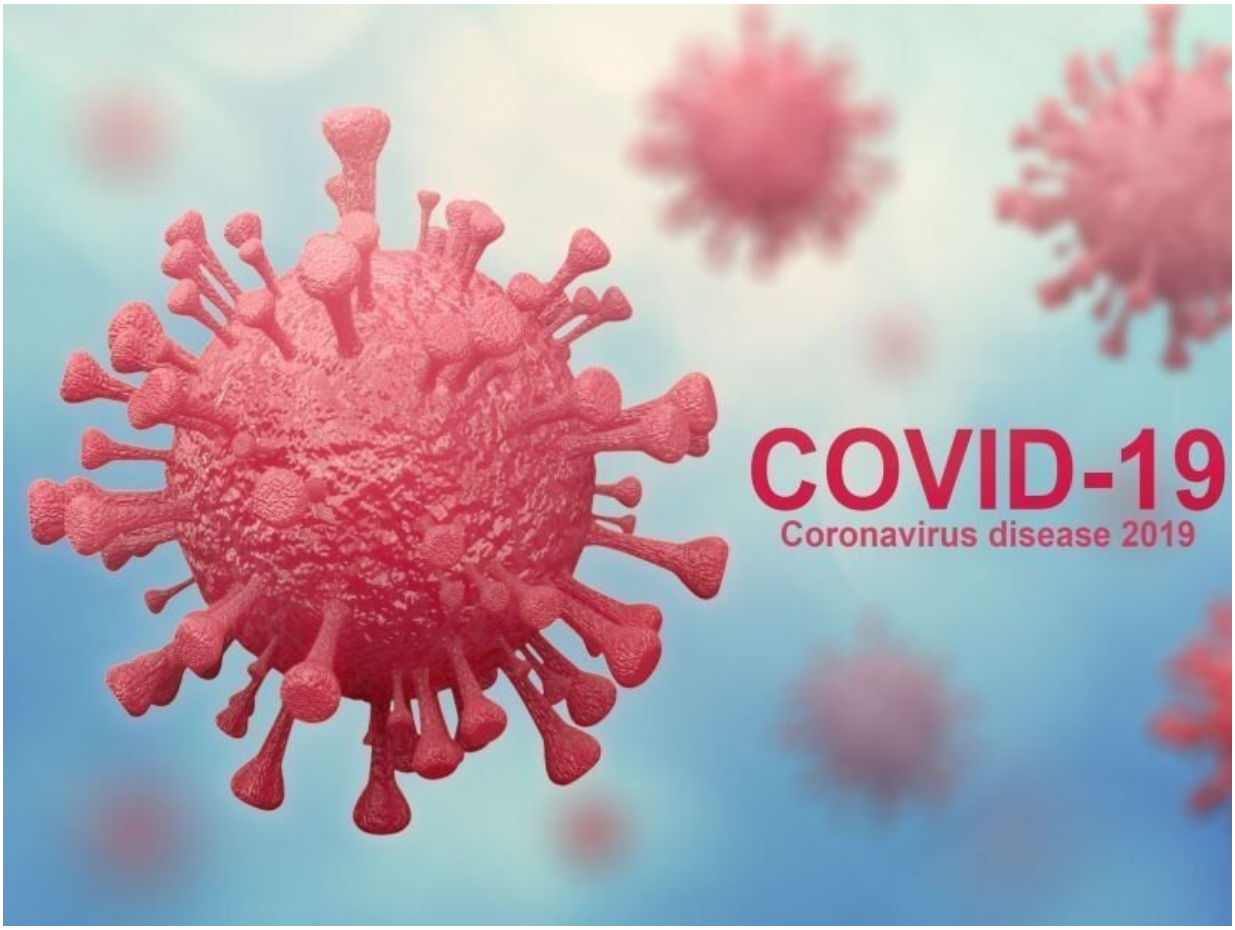

An experimental COVID-19 vaccine could potentially provide universal

protection against future COVID variants as well as other coronaviruses—maybe even the ones responsible for the common cold. And it's dirt cheap—less than $1 a dose, researchers say.

The vaccine targets a part of the COVID virus' spike protein that appears to be highly resistant to mutation and is common across nearly all coronaviruses, said senior researcher Dr. Steven Zeichner. He is a professor of pediatric infectious disease with the University of Virginia, in Charlottesville.

In animal studies, the COVID vaccine protected pigs against two separate diseases caused by two types of coronavirus, COVID-19 and porcine epidemic diarrhea virus (PEDV), according to results published online recently in the *Proceedings of the National Academy of Sciences*.

The two coronaviruses "are related, but they're distant cousins," Zeichner said. "The implication is if a COVID vaccine could protect a pig against PEDV, the likelihood is pretty good that it could provide broad protection against many different COVID variants."

These results represent a "great opportunity to develop universal coronavirus vaccines," said Dr. Amesh Adalja, a senior scholar at the Johns Hopkins Center for Health Security, in Baltimore.

"Other coronaviruses cause approximately 25% of our common colds, and are also major emerging infectious disease threats," Adalja said. "Being able to take coronaviruses off the table as a biological threat would be a major advantage, and a universal vaccine would be the best means to do so."

Cost is another advantage of the new vaccine.

The experimental vaccine is based on genetically modified bacteria,

which can be mass-produced at a fraction of the cost of currently approved COVID-19 vaccines, Zeichner said.

The mRNA COVID-19 vaccines now in use cost about $10 a dose, a price that could be prohibitive in developing countries, he noted.

But bacteria-based vaccines for cholera and pertussis can be brewed in large quantities on the cheap. A South Korean company reportedly made 6 million doses of cholera vaccine in one year using a single 100-liter fermenter, at a cost of less than $1 a dose, Zeichner said.

"A 100-liter fermenter is trivially small," he said. "That's the size of the gas tank in your car. It's the volume of a filing cabinet in your office."

A 1,500-liter vat—the size of the one at your local brew pub—could exponentially scale up production and bring the per-dose cost even lower, Zeichner said.

"If you have two or three or four, pretty soon you get enough vaccine to immunize everybody in the world," he added.

Zeichner and his colleagues designed the vaccine to go after a portion of the COVID virus' spike protein called the "viral fusion peptide," which is essentially universal among coronaviruses. The spike protein is what the virus uses to invade human cells.

"In all of the sequences that have been obtained so far for SARS-CoV-2 [the virus that causes COVID-19], that region of the spike protein doesn't show any changes at all," Zeichner said. "If it hasn't shown any changes so far, then it's unlikely to start showing changes in the future."

If the new target proves effective in follow-up research, companies with COVID-19 vaccines already on the market might want to incorporate it

into potential future "booster" doses, Zeichner said.

Current vaccines work by tricking human cells into producing incomplete versions of the COVID spike protein, to which the immune system responds and builds a defense for future attack.

The vaccines from Pfizer and Moderna do this by introducing genetic information directly into cells via messenger RNA, while the vaccines from Johnson & Johnson and AstraZeneca use a hollowed-out adenovirus to harmlessly infect the cells.

Both types of vaccine "actually have to enter into cells and then instruct the cells to make the vaccine antigens," Zeichner explained.

Taking a different approach

This experimental vaccine takes another tack. Researchers genetically engineer E. coli bacteria, removing the parts that make people sick and adding the coronavirus spike protein target to the surface of the bacteria.

The bacteria are then killed off and injected into the person or animal, where the immune system recognizes it as an invader and mounts a defense. The bacteria itself prompts the immune response, rather than something produced by human cells.

"All that you need to do that is you take your bacteria, you grow it and then you inactivate it with a little bit of formaldehyde, and that's your vaccine," Zeichner said.

Such bacteria-based vaccines—called killed whole-cell vaccines—have been around for a century and only require refrigeration, he noted, making them much easier to transport than the deep-frozen mRNA vaccines.

While the early results are promising, Zeichner said that more work is needed on the experimental vaccine.

The vaccine did not prevent infection, but it did protect the pigs from developing severe symptoms. It also primed the immune system of the pigs to mount a more vigorous response to future infection.

Researchers now need to tune in the best dose, the best route for administering the vaccine and the best schedule, Zeichner said. They also want to experiment with other substances that could be added to further boost immune response.

All that will be done in animal studies before the team moves on to humans, he said.

Dr. William Schaffner is a professor of infectious diseases at Vanderbilt University Medical Center in Nashville, Tenn. He said, "Long journeys begin with first steps, and these are first steps. That said, this is very innovative. We have no idea whether it will work, but those preliminary data are exciting. And the notion that you could create a vaccine that has the capacity to prevent a whole spectrum of variants is very exciting, of course."

Schaffner noted that two decades of research has gone into the search for a universal flu vaccine, "and we're not there yet. But maybe it will work for COVID."

More information: Denicar Lina Nascimento Fabris Maeda et al. Killed whole-genome reduced-bacteria surface-expressed coronavirus fusion peptide vaccines protect against disease in a porcine model, *Proceedings of the National Academy of Sciences* (2021). DOI: 10.1073/pnas.2025622118