Universal ‘pan coronavirus vaccine’? Scientists believe it’s possible within 2-3 years

Masks are coming off and we’re venturing back into the world, thanks largely to vaccines and natural immunity. Still, viral evolution continues. SARS-CoV-2 will continue to spawn mutations that will gather, with older mutations, into ever new variants.

But two or three years from now, universal (“pan”) coronavirus vaccines will likely head off another pandemic, quelling COVID-24, should it materialize, into nothing worse than a bad cold.

Efforts to create universal coronavirus vaccines began shortly after the pandemic began. But how daunting is the task, given the difficulty of developing universal vaccines against influenza and HIV? Like SARS-CoV-2, those viruses have RNA as their genetic material. They can’t repair the replication errors that give rise to mutations, like DNA can.

So why, then, do experts think a “pan-CoV” vaccine is even possible?

The main reason is that flu viruses and HIV mutate two to four times faster than does SARS-CoV-2. Perhaps the new virus seems to be mutating like crazy because we’re paying such close attention. A new COVID variant makes instant headlines, even before reports have been peer-reviewed, let alone published. But a new version of a flu virus? It doesn’t make the news until a seasonal vaccine comes up short – like now.

Consider the particulars of the three viruses.

Flu blues

This year’s flu vaccine was a bust, offering “non-significant effectiveness of 16% against the predominant strain,” according to the CDC.

The surface of an influenza virus – what the immune system “sees” first – differs from the spike triplets that festoon SARS-CoV-2. Dotting the surface of a flu virus are two types of glycoproteins. Hemagglutinin (H) comes in 18 varieties and neuraminidase (N) in 11. Names of the virus reflect these surface features. The 1918 pandemic and swine flu of 2009 were H1N1; 2004’s bird flu was H5N1.

The H and N varieties form viral subtypes, and combinations of subtypes build flu virus strains. Vaccines contain two A strains and one B, which are the ones capable of causing epidemics or pandemics.

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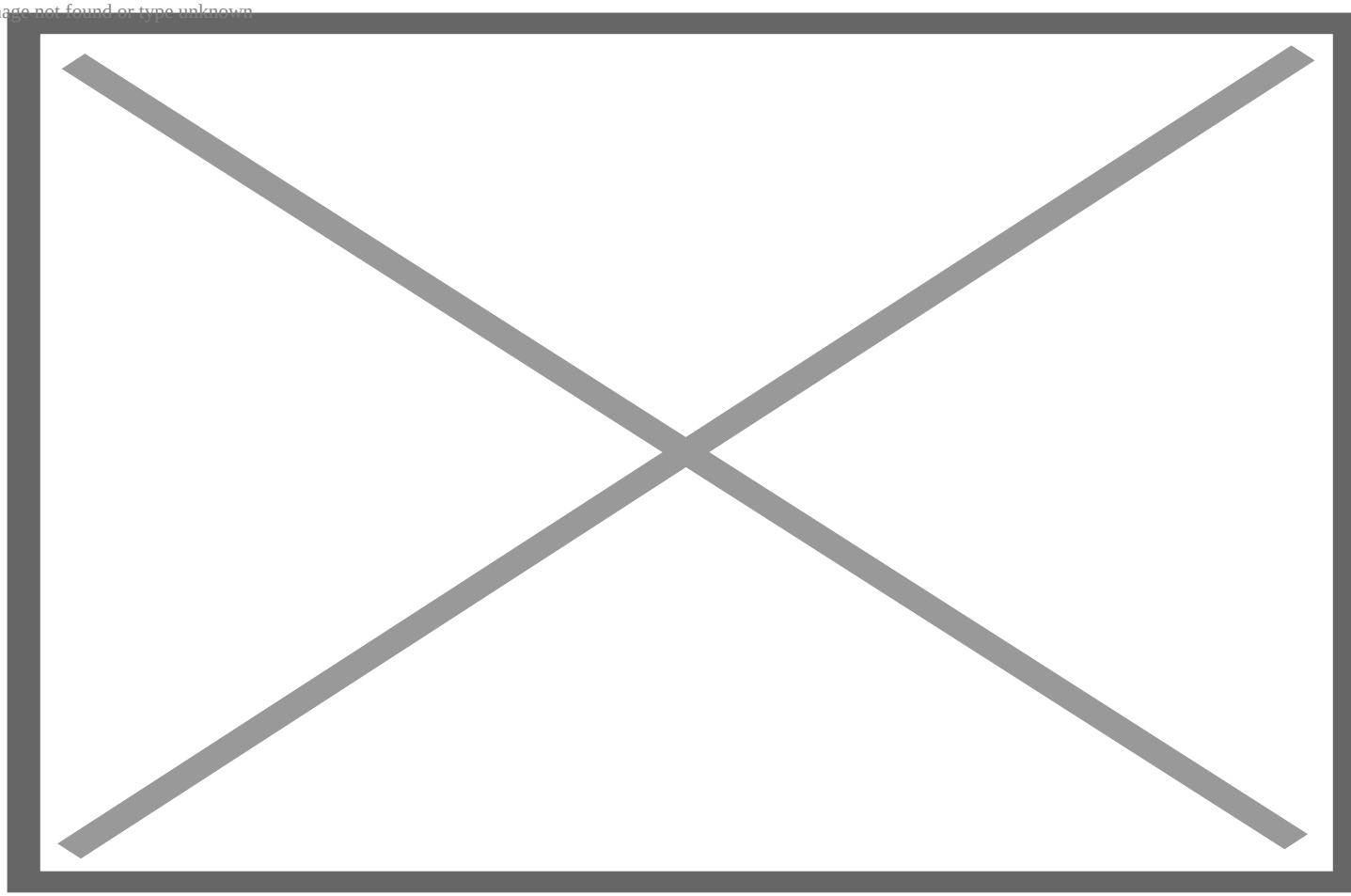

Credit: Burschik/Wikipedia

When a flu virus alters the combinations of its H and N surface glycoproteins, the change is termed a “shift”. It’s big.

Single RNA base mutations also happen, and these changes constitute viral “drift.” Shifting and drifting create a notoriously changeling virus. Seasonal changes reflect what’s happening among the bird populations in Asia where the viruses gestate.

Universal flu vaccines need to target a viral part that isn’t prone to change. One candidate is the stalk-like region of a hemagglutinin. It tends to be the same from strain to strain, whereas the heads vary yearly and that’s what vaccines traditionally target. Hemagglutinin enables the virus to enter a host cell. Other vaccines present the immune system with several H heads or combinations of flu virus pieces.

In 2018 the National Institute of Allergy and Infectious Disease (NIAID) started the Universal Influenza Vaccine Strategic Plan. Promising results from a phase 1 clinical trial for a vaccine that consists of H heads from bird flu viruses and stalks that many strains share, from Florian Krammer at Icahn School of Medicine at Mount Sinai and his team, appear in Nature Medicine.

An HIV/AIDS vaccine – Impossible?

“We hope to have a vaccine ready for testing in about two years,” said HIV co-discoverer Robert Gallo in 1984, of AIDS. He spoke too soon, for HIV presents “unique challenges to vaccine development,” according to historyofvaccines.org. The fact that HIV disables the very immune response that a vaccine is supposed to boost has stymied efforts. Here here is a great review of why we still don’t have an HIV/AIDS vaccine.

Like bait attracting fish, a vaccine presents part of a pathogen to awaken an immune response. The recipe may be a live but weakened virus or bacterium, a dead pathogen, or its parts.

Whatever a vaccine is, evaluating it requires a way to measure a response. On the population level, this means comparing two groups of people, one vaxxed and one not, over months or years of exposure in the community. Those epidemiological data are backed up with measurements of facets of the immune response, called “correlates of protection.”

The most common correlate of protection is antibody level, because antibodies are an early defense and the proteins are fast and cheap to measure in blood serum. The more lasting activation of T and B cells, which control production of antibodies, cytokines, and even directly kill pathogens, is much more cumbersome and expensive to check – they’re cells, not proteins in blood.

HIV doesn’t offer correlates of protection to measure because it cripples the immune response. There is no natural immunity to HIV as there is to SARS-CoV-2 from its cousin coronaviruses. And the lack of an animal model for HIV has hampered vaccine development too. Plus, HIV can lie dormant in a human body for a long time. Fortunately the antiretrovirals have been a huge success, an alternative to vaccines.

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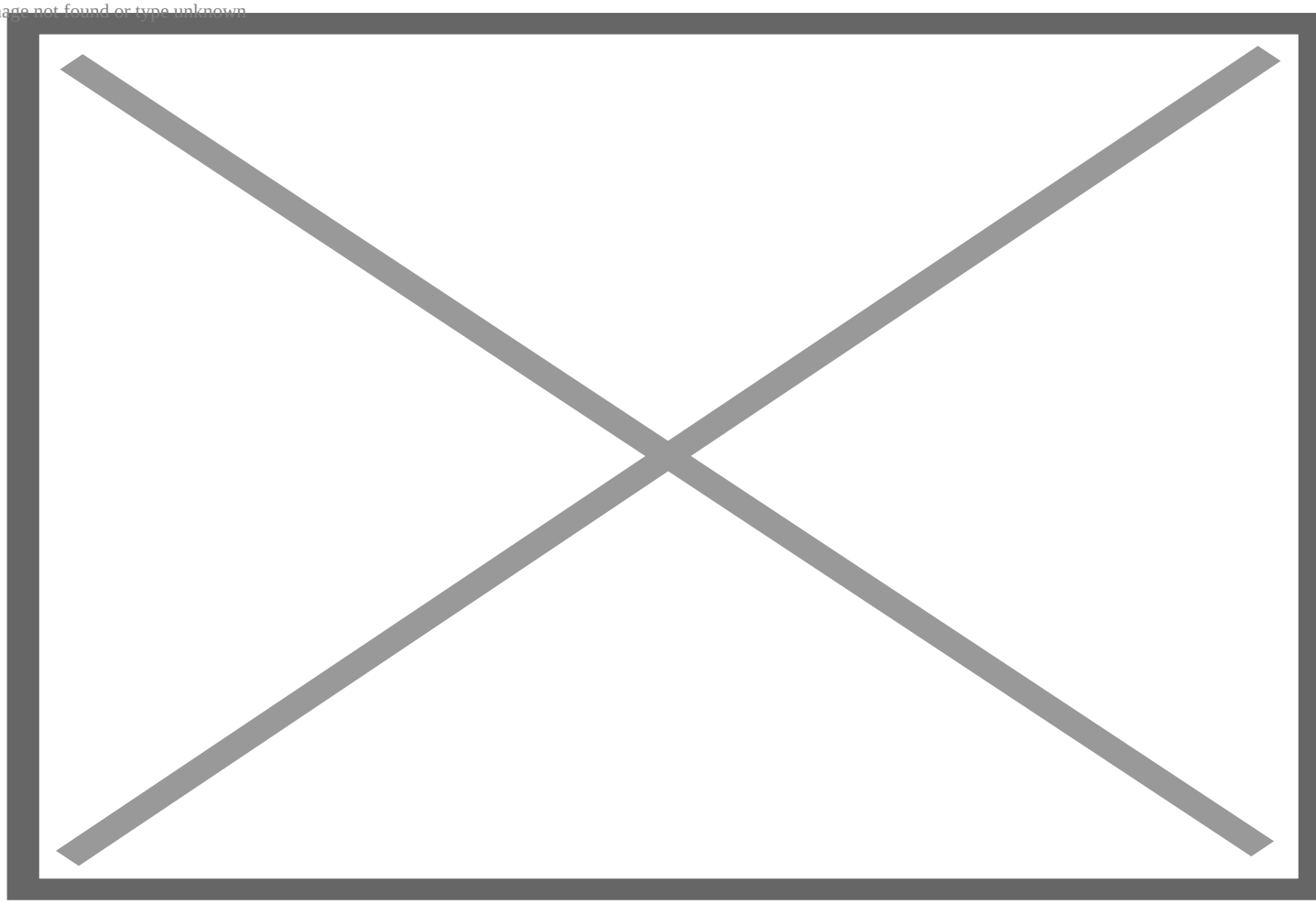

Credit: Getty Images

Why do we need a pan coronavirus vaccine?

Developing a pan coronavirus vaccine presents dual challenges: targeting viral parts that are retained in all variants, yet also hitting the most changeable part. That's the receptor binding domain, a small but key region of the spike protein that actually propels the virus inside our cells as two parts of the spike split. A pan approach offers better future protection, anticipating changes, than what's been dubbed the whack-a-mole approach of reinventing COVID-19 vaccines every time a new variant shows up and sweeps the world.

Yet even with our intimate knowledge of SARS-CoV-2 and our powerful predictive algorithms, science doesn't provide a crystal ball. We can't model every combination of events that could happen. And so a pan coronavirus vaccine should more realistically be called "broad spectrum," not truly universal, experts say. Even if not all encompassing, such a vaccine would be a deterrent to the diverse coronaviruses that continue to circulate among bats and can jump to and from plenty of other species, as well as the constant generation, recombination, and persistence of mutations in the virus.

We don't even know how many variations on the coronavirus theme are out there. When computational biologist Artem Babaian was recently between jobs, he invented a way to search NIH genome databases for an enzyme unique to RNA viruses, reported in Nature. He perused almost 132,000 entries and identified nine novel coronaviruses. They came from odd places, as these viruses tend to do: several fishes, a seahorse, a salamander, and an eel.

Because SARS-CoV-2 is not as severe a shape shifter as a flu virus, nor does it shut down the immune response like HIV – in fact, it may rev it up too much – many efforts are underway to develop a COVID vaccine. NIAID announced a new round of funding on September 28, 2021.“ These new awards are designed to look ahead and prepare for the next generation of coronaviruses with pandemic potential," said director Anthony Fauci.

Variations on a pan coronavirus vaccine

The spikes, which the virus uses to latch onto and pierce our cells, are obvious vaccine targets. Researchers have eclectic approaches to breach this barrier.

At least two research groups are retooling ferritin, a protein in the blood that binds and transports iron, to instead carry coronavirus spike proteins, or just the receptor-binding domain. Another strategy attaches spikes from up to 8 different coronaviruses to proteins from Strep bacteria. The antibody response targets more than 8 coronaviruses, which indicates a broad attack against antigens (surface molecules) that many types of coronaviruses share. The goal is to protect against variants that haven't yet arisen.

An mRNA-based experimental vaccine consists of what the researchers call "scrambled coronavirus spikes" that include the receptor-binding domain and two other parts of the spike.

Still another strategy, reminiscent of the search for a universal flu vaccine based on stalks, targets the "stem-helix" part of a coronavirus's spike that gloms onto our cells. And others transcend the spike altogether. A vaccine from French company Osivax targets the nucleocapsid proteins that protect the delicate genetic material, the viral RNA.

Coda

We haven’t seen the last of COVID-19, which is why in my writing, I retain the 19. We can’t know when it will re-emerge, or exactly what it will look like. But with an arsenal of broad-spectrum vaccines in the works, next time, we’ll be better prepared.

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