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Scientists have begun the race to create a single vaccine that protects us from all future coronaviruses, with human trials starting soon, finds Graham Lawton

The coronavirus sweeping around the world isn’t the first to make the leap into humans and it won’t be the last. Vaccines against SARS-CoV-2 were developed in record time and are performing well. But now we urgently need a different kind of vaccine, say scientists: one that will protect us against other coronaviruses, even those we haven’t met yet.

It is a daunting challenge, yet work has already begun on creating such a universal vaccine, with the first human trials of potential candidates planned to start later this year.

In the past 20 years, humanity has endured three outbreaks of disease caused by novel coronaviruses: SARS, MERS and now Covid-19. The first two are very deadly – up to 35 per cent of people who catch MERS, and 10 per cent of those with SARS, die – but they aren’t very transmissible. Covid-19 is highly transmissible, but not as deadly: so far, up to about 1 per cent of people who have caught it have died.

With a number of other coronaviruses out there poised to make the leap from animals into humans, there will almost certainly be a fourth. And as Wayne Koff, CEO of global consortium the Human Vaccines Project, points out, if the next coronavirus is as transmissible as SARS-CoV-2 and as deadly as the viruses that cause SARS or MERS, “within a year we could have 100 million dead”.

“*If the next coronavirus is as transmissible as this one and as deadly as the MERS one, 100 million could die*”

The solution to this threat is obvious, says Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases (NIAID). “We would like to develop a universal coronavirus vaccine for all coronaviruses,” he said at an online meeting run by the New York Academy of Sciences this month.

This is easier said than done. A universal coronavirus vaccine would need to identify a region of the virus that is so integral to its survival that it is conserved across all coronaviruses, and doesn’t change as viruses mutate.

Scientists believe such highly conserved regions could be universal epitopes – immune system-stimulating regions of the virus – that could be used to make a vaccine that is effective against multiple coronaviruses.

So far, it isn’t even clear that we can make a vaccine that protects against all variants of SARS-CoV-2, let alone coronaviruses in general. But there are signs that a universal vaccine may be on the cards.

Calls to create one began in 2014, when Abul Islam and Refat Sharmin at the University of Dhaka in Bangladesh discovered an epitope within an enzyme that was universal across all known human coronaviruses, and suggested it as a target for a universal vaccine. It was published in *BMC Bioinformatics*, but wasn’t followed up.

According to Luca Giurgea at NIAID, scientists now accept the need to at least try. In May 2020, he and two colleagues published an opinion piece in the journal *NPJ Vaccines* entitled “Universal coronavirus vaccines: the time to start is now”. They urged the world not to just focus on vaccines for SARS-CoV-2, but to think bigger.

“We were confronted with some scepticism,” says Giurgea. “Now that we are starting to get data suggesting some of the vaccines have lower efficacy against the new variants, we are finally seeing a considerable shift in attention towards more broadly protective vaccines.”

**Hidden targets**

The good news is that present and future coronaviruses are likely to have common features that a universal vaccine could exploit. As well as the epitope discovered by Islam and Sharmin in 2014, there are also spike proteins that coronaviruses use to enter our cells. Those of SARS-CoV, the virus that causes SARS, and SARS-CoV-2 are about 78 per cent identical in terms of the sequence of their component amino acids.

Such highly conserved regions must be biologically important and so present a tempting target for vaccines because coronaviruses are unlikely to be able to escape them by mutating, given such changes would probably render the virus inactive.

Immunological evidence also suggests that there are conserved aspects of several coronaviruses, given that antibodies against one can protect against another. For instance, antibodies from people who have recovered from SARS are...
sometimes protective against SARS-CoV-2, and vice versa. It is also possible to generate antibodies in mice that are effective against SARS, MERS and covid-19. Likewise, animals immunised against SARS-CoV gained resistance to SARS-CoV-2, as well as a SARS-like bat coronavirus that has previously been identified as a potential threat to humans.

The discovery of these broadly neutralising antibodies, which can recognise epitopes from several different coronaviruses, strongly suggests that a universal vaccine is possible, says vaccinologist Dennis Burton at the Scripps Research Institute in La Jolla, California.

**Human trials**

For example, Ralph Baric at the University of North Carolina School of Medicine and his colleagues isolated antibodies from a person who had been infected with SARS-CoV and identified those that were broadly neutralising against other coronaviruses, including SARS-CoV-2. They then tweaked the antibodies using genetic engineering to make them even more potent. Finally, they analysed these supercharged antibodies to work out which region of the spike protein they bound to as this must be highly conserved, and could be the Achilles heel of the virus.

“There are clearly major cross-neutralising epitopes that exist and if we’re going to develop broad-based vaccines, we need to identify where those epitopes are,” says Baric.

Another approach is to make artificial proteins bearing features of spike proteins from several human and animal coronaviruses. An experimental vaccine based on this approach has already been shown to induce broad immunity against multiple coronaviruses in a mouse model. This result is “rather promising”, says Giurgea.

Researchers at Los Alamos National Laboratory in New Mexico also have a universal vaccine in their sights. Bette Korber, who leads its universal coronavirus vaccine research, says there are a number of highly conserved regions across the whole group of coronaviruses that include SARS-CoV, SARS-CoV-2, MERS-CoV (the virus responsible for MERS) and some viruses that cause the common cold.

Studies show that these regions can be used to provoke a T-cell immune response in mice. T-cells kill infected cells and aren’t normally the primary goal of a vaccine. However, it might be useful to add these highly conserved epitopes to existing vaccines to get a broader immune response.

Finally, there are a handful of biotech companies that are taking steps towards a commercial universal vaccine. ConserV Bioscience in the UK says it is developing an mRNA vaccine that covers the full spectrum of coronaviruses, including those that cause the common cold, although it hasn’t revealed exactly how its vaccine works.

The goal is to develop a vaccine that could be given to people every few years to head off a future pandemic, says CEO Kimbell Duncan. The vaccine is in preclinical testing and could enter early human trials this year, he adds.

Another company, VBI Vaccines in Massachusetts, says it is planning to begin human trials later this year of a universal vaccine that targets SARS-CoV, SARS-CoV-2 and MERS-CoV spike proteins.

The race to create a vaccine for SARS-CoV-2 was won in record time, but the next race is just starting, and not a moment too soon. “It’s very easy to imagine highly pathogenic coronavirus strains with 10 to 15 per cent mortality rate that are nearly as transmissible as covid-19,” says Baric. “There’s some serious threat out there and we really, really need to pay attention to it.”