DNA VACCINES: A NOVEL APPROACH TO THE PANDEMIC

Management of the COVID-19 pandemic RELIES ON VACCINES produced using a variety of approaches.

Japan's COVID-19 vaccination programme has been slow in comparison to other developed countries. By the end of May 2021 only 4% of the population had been vaccinated, by the end of August, less than half the population were fully dosed. This was partly due to difficulties with supply of imported vaccines, and because the Japanese approval process includes a requirement for a domestic clinical trial involving Japanese citizens.

IT IS LIKELY THAT WE WILL NEED AT LEAST ONE, MAYBE TWO VACCINES A YEAR AGAINST CORONAVIRUS

Ryuichi Morishita, founder of AnGes, a gene-based medical company, and professor of clinical gene therapy at the Center of Medical Innovation and Translational Research at Osaka University, believes a solution can be found close to home: "Domestic vaccine production would help Japan to respond faster to the spread of new viruses," he says.

There are four main types of COVID-19 vaccines in use and in development: whole attenuated virus vaccines; subunit vaccines; viral vector vaccines; and nucleic acid vaccines. All of them aim to stimulate an immune response against the spike protein. This protein is found on the surface of SARS-CoV-2 (the virus responsible for COVID-19), it binds to angiotensin-converting enzyme 2 (ACE2) proteins on the surface of host cells which allow the virus to enter the cell and cause infection.

"The Government of Japan is supporting the development of various vaccination approaches including the development of the DNA vaccine that we are working on," Morishita says. Nucleic acid vaccines deliver the instructions to make specific virus proteins directly into human cells as either RNA or DNA. The advantages of such vaccines are that they are easy to make in bacteria, large amounts can be produced within weeks, and they are relatively safe, since no pathogens are used in the vaccine manufacturing process. The first mRNA vaccines approved for use in humans — the Pfizer/BioNTech and Moderna COVID-19 vaccines — are being rolled out around the world.

A downside of RNA vaccines is that they need to be kept at ultra-cold temperatures, -60°C or lower, which can limit their distribution in countries without specialized cold storage equipment. By contrast, Morishita says DNA vaccines are very stable. "They can be kept in a standard commercial refrigerator for up to five years at least."

Although the safety of DNA vaccines has been studied for more than a decade and have raised no safety concerns in humans, it was only on 20 August 2020 that the first, a COVID-19 vaccine, was approved in India for use in humans. There are currently no approved DNA vaccines in Japan for humans. This may be about to change. The recent conditional approval in Japan of the drug Collatagene, which contains a small, circular DNA molecule, called a plasmid, with the gene for hepatocyte growth factor, for the treatment of critical lower limb ischaemia, could pave the way for regulatory approval of other DNA plasmid-based therapies, including DNA vaccines.

In March 2020, AnGes began developing a DNA plasmid vaccine that contains the gene encoding the coronavirus spike protein. Host cells recognize the DNA fragment and transcribe it into an RNA fragment from which the spike protein is produced.

"With this DNA vaccine, our cells temporarily become factories producing the spike protein, that is recognized by the immune system as foreign, leading to long-lasting protection," Morishita explains.

Furthermore, due to the presence of dendritic cells in the dermis, subcutaneous tissue may be a better delivery site for DNA vaccines than the muscles targeted in injections. AnGes is working with Daicel Corp, an Osaka-based chemical company on phase I/II trials to test the feasibility of delivering their vaccine via a gunpowder-based needleless injection system. This could allow them to use smaller doses, which may allow them to supply more vaccines.

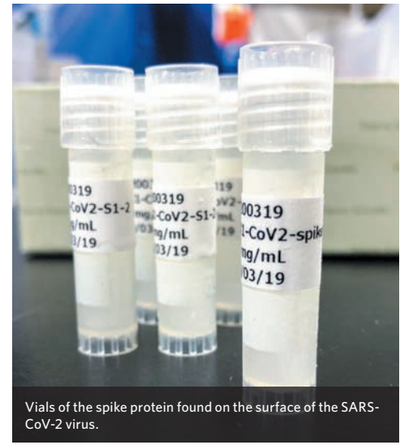
Importantly, the DNA vaccine is cheap to produce, and can easily be tweaked to tackle new viruses and virus variants, which are an emerging threat globally. Vaccine makers are preparing for the production of new booster doses and Morishita believes this is where the AnGes vaccine may fit in. The company is trying to modify the DNA sequence of the spike protein in their vaccine to work against variants of concern, including the delta, gamma, and beta strains of SARS-CoV-2.

"If our DNA vaccine can increase the neutralizing antibody to the same level as the Pfizer/Moderna vaccines after the initial vaccination, it might be efficient as a booster vaccine following them."

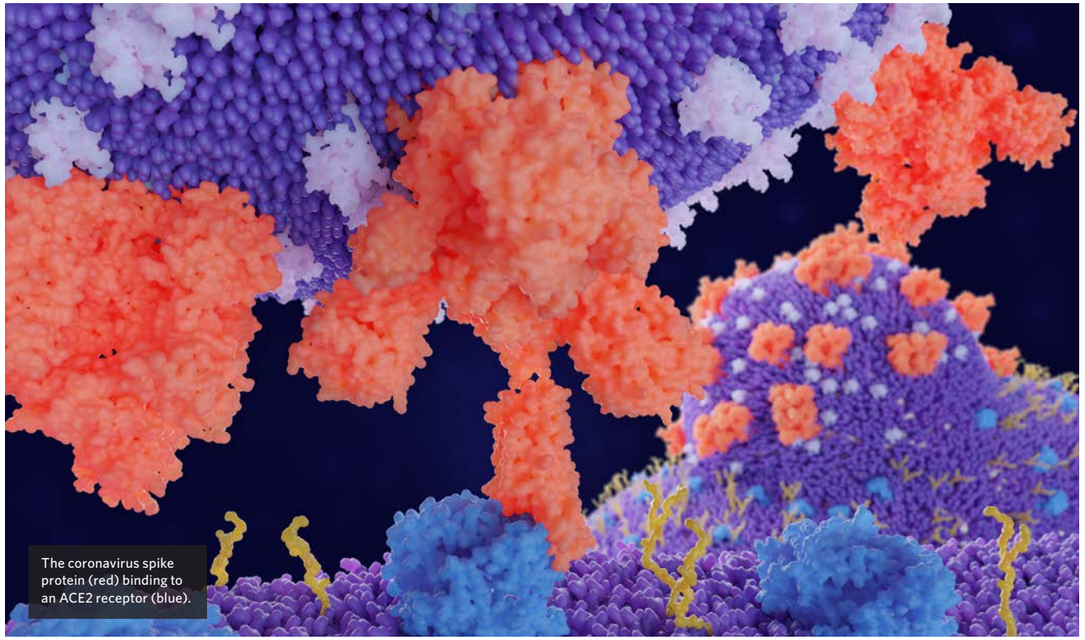
At the latest COVAX Summit hosted by the Government of Japan and Gavi, the Vaccine Alliance, Japan demonstrated its commitment to global equitable access to COVID-19 vaccines by pledging an additional US$800 million towards purchasing vaccines for 92 low-and-middle-income countries. The domestic production of SARS-CoV-2 DNA vaccines will not only help reduce reliance on imported vaccines, but will also be key to ensure vaccine supply meets demand in the ASEAN region.

"It is likely that we will need at least one, maybe two vaccines a year against coronavirus," Morishita says. Booster shots from Japan may be a useful tool in the global effort to overcome the pandemic. ■

Needleless injections targeting subcutaneous tissue may be a better option for DNA vaccines than intramuscular injections (pictured).



Vials of the spike protein found on the surface of the SARS-CoV-2 virus.



The coronavirus spike protein (red) binding to an ACE2 receptor (blue).

AnGes

www.anges.co.jp/en

Advertiser retains sole responsibility for content