THE RACE FOR CORONAVIRUS VACCINES

By Ewen Callaway; design by Nik Spencer.

More than 90 vaccines are being developed against SARS-CoV-2 by research teams in companies and universities across the world. Researchers are trialling different technologies, some of which haven’t been used in a licensed vaccine before. At least six groups have already begun injecting formulations into volunteers in safety trials; others have started testing in animals. Nature’s graphical guide explains each vaccine design.

VACCINE BASICS: HOW WE DEVELOP IMMUNITY

The body’s adaptive immune system can learn to recognize new, invading pathogens, such as the coronavirus SARS-CoV-2.

Coronavirus infection*

The virus uses its surface spike protein to lock onto ACE2 receptors on the surface of human cells. Once inside, these cells translate the virus’s RNA to produce more viruses.

1. Virus enters the body

2. Virus enters a cell

3. Virus fuses with vesicle and its RNA is released

4. Virus assembly

Viral RNA translated into proteins

5. Virus release

Immune response*

Specialized ‘antigen-presenting cells’ engulf the virus and display portions of it to activate T-helper cells. T-helper cells enable other immune responses: B cells make antibodies that can block the virus from infecting cells, as well as mark the virus for destruction. Cytotoxic T cells identify and destroy virus-infected cells.

Virus

Viral vector

Nucleic acid

Protein-based

Other*

Weakened

Weakened

Weakened

Weakened

Replicating

Non-replicating

DNA

Protein subunit

RNA

Virus-like particles

Number of vaccines in development

0 5 10 15 20 25 30 35

* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

AN ARRAY OF VACCINES

All vaccines aim to expose the body to an antigen that won’t cause disease, but will provoke an immune response that can block or kill the virus if a person becomes infected. There are at least eight types being tried against the coronavirus, and they rely on different viruses or viral parts.

VIRUS VACCINES

At least seven teams are developing vaccines using the virus itself, in a weakened or inactivated form. Many existing vaccines are made in this way, such as those against measles and polio, but they require extensive safety testing. Sinovac Biotech in Beijing has started to test an inactivated version of SARS-CoV-2 in humans.

Weakened virus

A virus is conventionally weakened for a vaccine by being passed through animal or human cells until it picks up mutations that make it less able to cause disease. Codagenix in Farmingdale, New York, is working with the Serum Institute of India, a vaccine manufacturer in Pune, to weaken SARS-CoV-2 by altering its genetic code so that viral proteins are produced less efficiently.

Inactivated virus

In these vaccines, the virus is rendered infectious using chemicals, such as formaldehyde, or heat. Making them, however, requires starting with large quantities of infectious virus.

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**NUCLEIC-ACID VACCINES**

At least 20 teams are aiming to use genetic instructions (in the form of DNA or RNA) for a coronavirus protein that prompts an immune response. The nucleic acid is inserted into human cells, which then churn out copies of the virus protein; most of these vaccines encode the virus’s spike protein.

RNA- and DNA-based vaccines are safe and easy to develop: to produce them involves making genetic material only, not the virus. But they are unproven: no licensed vaccines use this technology.

**VIRAL-VECTOR VACCINES**

Around 25 groups say they are working on viral-vector vaccines. A virus such as measles or adenovirus is genetically engineered so that it can produce coronavirus proteins in the body. These viruses are weakened so they cannot cause disease. There are two types: those that can still replicate within cells and those that cannot because key genes have been disabled.

**Protein subunits**

Twenty-eight teams are working on vaccines with viral protein subunits — most of them are focusing on the virus’s spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven’t been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.

**VLP**

Empty virus shells mimic the coronavirus structure, but aren’t infectious because they lack genetic material. Five teams are working on ‘virus-like particle’ (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.

**PROTEIN-BASED VACCINES**

Many researchers want to inject coronavirus proteins directly into the body. Fragments of proteins or protein shells that mimic the coronavirus’s outer coat can also be used.

**Replicating viral vector (such as weakened measles)**

The newly approved Ebola vaccine is an example of a viral-vector vaccine that replicates within cells. Such vaccines tend to be safe and provoke a strong immune response. Existing immunity to the vector could blunt the vaccine’s effectiveness, however.