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How Gamaleya's Vaccine Works

9-12 minutes

The Gamaleya Research Institute, part of Russia's Ministry of Health, developed a coronavirus vaccine known as **Sputnik V** or **Gam-Covid-Vac**. Gamaleya published a study in February showing that two doses of the vaccine had an efficacy rate of 91.6 percent. Russia is using it in a mass vaccination campaign, and the vaccine has been approved for emergency use

in dozens of other countries.

In May, a one-dose version dubbed "Sputnik Light" was authorized for emergency use in Russia, with an announced efficacy of 79.4 percent.

A Piece of the Coronavirus

The SARS-CoV-2 virus is studded with proteins that it uses to enter human cells. These so-called spike proteins make a tempting target for potential vaccines and treatments.

Sputnik V is based on the virus's genetic instructions for building the spike protein. But unlike the Pfizer-BioNTech and Moderna vaccines, which store the instructions in single-

stranded RNA, Sputnik V uses double-stranded DNA.

DNA Inside Adenoviruses

The researchers developed their vaccine from adenoviruses, a kind of virus that causes colds. They added the gene for the coronavirus spike protein gene to two types of adenovirus, one called Ad26 and one called Ad5, and engineered them so they could invade cells but not replicate.

Sputnik V comes out of decades of research on adenovirus-based vaccines. The first one was approved for general use last year — a vaccine

for Ebola, made by Johnson & Johnson. Some other coronavirus vaccines are also based on adenoviruses, such as one from Johnson & Johnson using Ad26, and one by the University of Oxford and AstraZeneca using a chimpanzee adenovirus.

Entering a Cell

After Sputnik V is injected into a person's arm, the adenoviruses bump into cells and latch onto proteins on their surface. The cell engulfs the virus in a bubble and pulls it inside. Once inside, the adenovirus escapes from the bubble and travels to the nucleus,

the chamber where the cell's DNA is stored.

The adenovirus pushes its DNA into the nucleus. The adenovirus is engineered so it can't make copies of itself, but the gene for the coronavirus spike protein can be read by the cell and copied into a molecule called messenger RNA, or mRNA.

Building Spike Proteins

The mRNA leaves the nucleus, and the cell's molecules read its sequence and begin assembling spike proteins.

Some of the spike proteins produced by the cell form spikes that migrate to its surface and stick out their tips. The

vaccinated cells also break up some of the proteins into fragments, which they present on their surface. These protruding spikes and spike protein fragments can then be recognized by the immune system.

The adenovirus also provokes the immune system by switching on the cell's alarm systems. The cell sends out warning signals to activate immune cells nearby. By raising this alarm, Sputnik V causes the immune system to react more strongly to the spike proteins.

Spotting the Intruder

When a vaccinated cell dies, the debris

contains spike proteins and protein fragments that can then be taken up by a type of immune cell called an antigen-presenting cell.

The cell presents fragments of the spike protein on its surface. When other cells called helper T cells detect these fragments, the helper T cells can raise the alarm and help marshal other immune cells to fight the infection.

Making Antibodies

Other immune cells, called B cells, may bump into the coronavirus spikes on the surface of vaccinated cells, or free-floating spike protein fragments. A few of the B cells may be able to lock onto

the spike proteins. If these B cells are then activated by helper T cells, they will start to proliferate and pour out antibodies that target the spike protein.

Stopping the Virus

The antibodies can latch onto coronavirus spikes, mark the virus for destruction and prevent infection by blocking the spikes from attaching to other cells.

Killing Infected Cells

The antigen-presenting cells can also activate another type of immune cell called a killer T cell to seek out and destroy any coronavirus-infected cells

that display the spike protein fragments on their surfaces.

Two Doses, or One

Some researchers worry that our immune systems could respond to an adenovirus vaccine by making antibodies against it, which would render a second dose ineffective. To avoid this, the Russian researchers used one type of adenovirus, Ad26, for the first dose, and another, Ad5, for the second.

A version of the vaccine known as Sputnik Light uses only the first dose, and skips the second injection.

Adenovirus-based vaccines for

Covid-19 are more rugged than the mRNA vaccines from Pfizer and Moderna. DNA is not as fragile as RNA, and the adenovirus's tough protein coat helps protect the genetic material inside. As a result, Sputnik V can be refrigerated and does not require very low storage temperatures.

Remembering the Virus

Gamaleya has announced that the two-dose Sputnik V has an efficacy rate of 91.4 percent, and the single-dose Sputnik Light has an efficacy rate of 79.4 percent. But the company has not published scientific papers with the full details.

Two color-coded doses of Sputnik V.Russian Direct Investment Fund, via EPA

It's not yet clear how long the vaccine's protection might last. The level of antibodies and killer T cells triggered by the vaccine may drop in the months after vaccination. But the immune system also contains special cells called memory B cells and memory T cells that may retain information about the coronavirus for years or even decades.

Vaccine Timeline

June, 2020 Gamaleya launches clinical trials of their vaccine, initially

called Gam-Covid-Vac.

Aug. 11 President Vladimir V. Putin announces that a Russian health care regulator had approved the vaccine, renamed Sputnik V, before Phase 3 trials had even begun. Vaccine experts decry the move as risky.

Aug. 20 Russia walks back its earlier announcement, saying the vaccine approval was a "conditional registration certificate" that depends on positive results from Phase 3 trials.

Russian President Vladimir Putin during a teleconference on Aug. 11.Alexei Nikolsky/EPA

Sept. 4 Gamaleya researchers publish the results of their Phase 1/2 trial. In a

small study, they found that Sputnik V yielded antibodies to the coronavirus and mild side effects.

Sept. 7 A Phase 3 trial begins in Russia.

Oct. 17 A Phase 2/3 trial launches in India.

Nov. 11 The Russian Direct Investment Fund announces the first preliminary evidence from their Phase 3 trial indicating that the vaccine is effective. Based on 20 cases of Covid-19 among the trial participants, Russian scientists estimate that the vaccine has 92 percent efficacy.

A vial of Gamaleya's vaccine.Fedja Grulovic/Reuters

November The Russian government begins offering Sputnik V within Russia in a mass vaccination campaign. But worry that the vaccine was rushed to approval leads to widespread hesitancy in the country.

December The Phase 3 trial reaches its final total of 78 cases. The efficacy rate was effectively unchanged, at 91.4 percent. Out of the 78 cases of Covid-19 in the trial, 20 were severe — and all 20 were in volunteers who received the placebo. In addition, the researchers announce that they found no serious side effects from the vaccine.

Dec. 11 The drugmaker AstraZeneca,

which is developing an adenovirus-based vaccine in partnership with the University of Oxford, joins forces with Gamaleya to see if combining their vaccine with Sputnik V would increase the efficacy of the Oxford-AstraZeneca vaccine.

Vials of the vaccine at a facility near Saint Petersburg, Russia.Anton Vaganov/Reuters

Dec. 24 The Associated Press reports that trial volunteers who suspect they received the placebo are dropping out to receive the vaccine now that it's widely available. The researchers running the trial reduce its planned size from 40,000 to 31,000 participants,

causing experts to worry that it will not have enough statistical power to reach strong conclusions about the safety and efficacy of the vaccine.

Dec. 22 Belarus becomes the first country outside of Russia to register Sputnik V.

Dec. 23 Argentina authorizes the vaccine for emergency use.

Vials of the vaccine in Rosario, Argentina.Agence France-Press

Dec. 24 AstraZeneca registers a Phase 1 trial for a combination of the Sputnik V and Oxford-AstraZeneca vaccines.

Preparing a dose in Moscow on Dec.

30.Natalia Kolesnikova/Agence France-Presse

January, 2021 Gamaleya begins a trial of a single-dose version of the vaccine, called Sputnik Light.

Feb. 2 Phase 3 trial results appear in the Lancet.

March 4 European regulators begin a rolling review of Sputnik V.

May 6 Russia announces that the one-dose version of the vaccine, called Sputnik Light, is authorized for emergency use and provides an efficacy of 79.4 percent.

Additional reporting by Yuliya Parshina-Kottas. Sources: National Center for

Biotechnology Information; Nature; Lynda Coughlan, University of Maryland School of Medicine.

Tracking the Coronavirus