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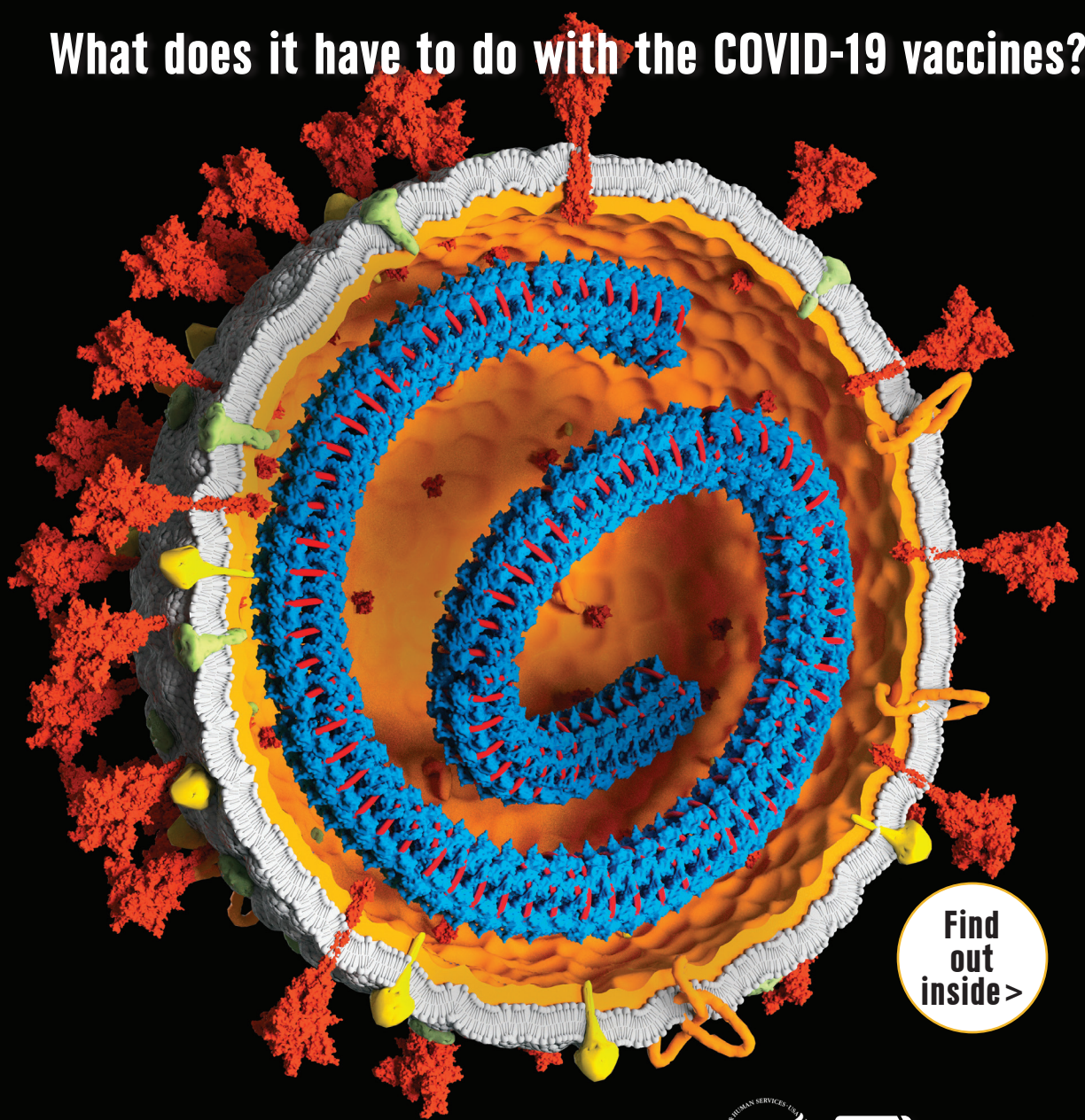
The Vaccine Science Issue

PATHWAYS

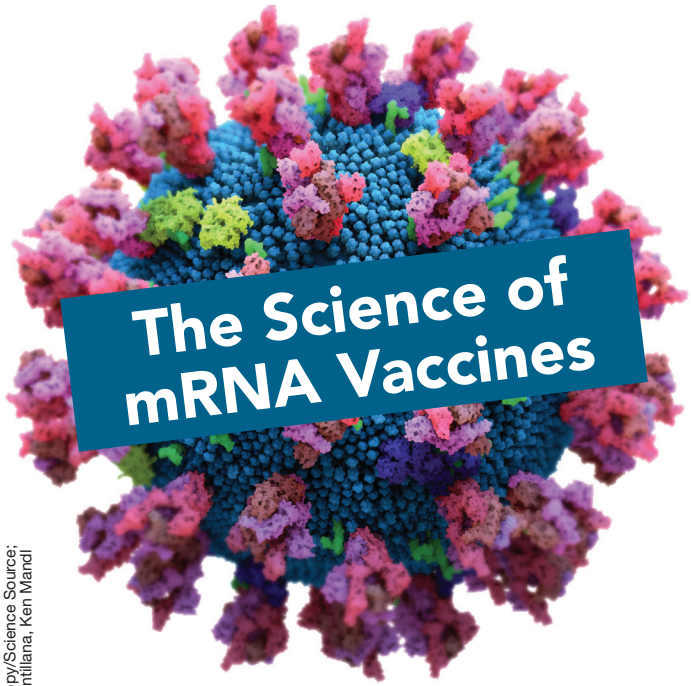
THE SPIKE PROTEIN

What does it have to do with the COVID-19 vaccines?



Find out inside >

NIH National Institute of General Medical Sciences



The Science of mRNA Vaccines

Read about vaccine research and other tools for preventing outbreaks

Vaccines are in the headlines a lot these days, but does it surprise you to know that vaccine science isn't new? Scientists around the world have been studying vaccines for more than 300 years. Fast-forward to today, we now have vaccines that can protect us from illness and death from infectious diseases like measles, polio, and—most recently—COVID-19. Scientists used a new method, built on years of research, to create one type of COVID-19 vaccine. Let's look at how it works.

mRNA Vaccines

A molecule called **messenger RNA**, or mRNA, is naturally found in every cell in your body. Cells use it to convey information about what types of proteins to manufacture so your body can function.

COVID-19 mRNA vaccines (including the Pfizer and Moderna vaccines) use mRNA to give your body important information to defend itself against COVID-19. Check out the infographic to learn how.

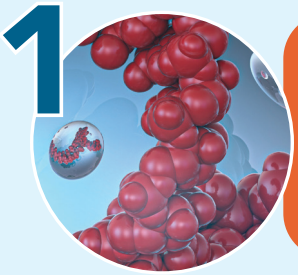
The Spike on Screen

When Dr. Kizzmekia Corbett's coronavirus vaccines team at the National Institutes of Health was tasked with addressing the COVID-19 outbreak, she felt prepared. "We knew exactly what to do, based on our past work," says Dr. Corbett, an expert immunologist,

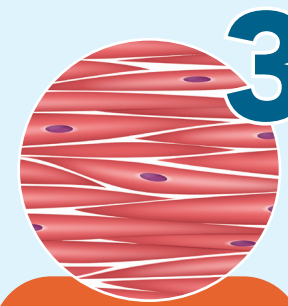
Illustrations: DESIGN CELLS/Science Source; LAGUNA DESIGN/Science Source; iStock; Juan Gaertner/Science Source; Dennis Kunkel Microscopy/Science Source; MEHAU KULYK/Science Source. Photos: Dr. Kizzmekia Corbett and Dr. Jason McLellan, courtesy of Dr. Corbett and Dr. McLellan; Dr. Mauricio Santillana, Ken Mandl

Journey of an mRNA Vaccine

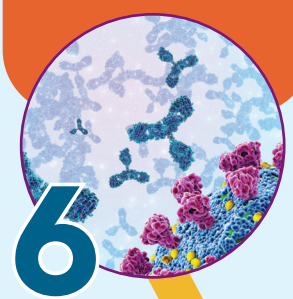
The SARS-CoV-2 virus (the virus that causes COVID-19) has a spike protein that it uses like a tool to break into and infect cells. But scientists have found a way to safely use this spike to develop the mRNA vaccine.



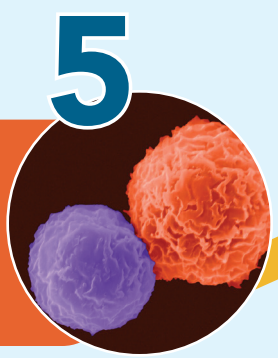
Scientists make copies of **mRNA** with instructions that tell the human body how to make **only** the outer ***spike protein*** of SARS-CoV-2.



The vaccine's mRNA instructions pass into **muscle cells** (near where a vaccine injection is given), and those muscle cells make copies of the spike protein.



If SARS-CoV-2 (and its telltale spike proteins) enter a vaccinated person's body, the immune system reacts with **antibodies** that defend against infection more swiftly than it otherwise could if it had never seen the spike protein.



The body eliminates the vaccine material. Special white blood cells called **memory cells** "remember" the spike protein and which antibodies to make if they happen upon the spike again.

Cover: Top image is an illustration of vaccine particles containing mRNA instructions for producing the spike protein portion of SARS-CoV-2. Main image is an illustration of the SARS-CoV-2 virus, with the spikes on the outside and the full RNA **genome** on the inside.

Wait! Is the spike protein dangerous?

NO

On its own, the spike protein is harmless and can be used as a tool to train your immune system to defend against the virus.

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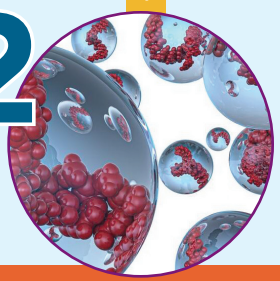

mRNA is packaged inside tiny globules called **lipid nanoparticles**. Lipids (fatty acids) are used as the vehicle because they:

- Protect the mRNA from breaking down
- Help it pass through cell membranes and into the body's cells

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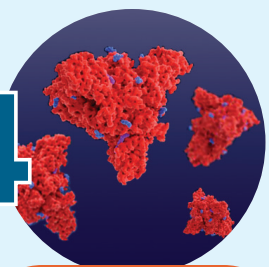


Though the spikes are harmless, the body's immune system recognizes them as **antigens** (foreign substances) and produces targeted antibodies to defend against them.

now an assistant professor at Harvard.

To develop a vaccine, Dr. Corbett and her team needed to identify the **antigen** (in this case, the spikes on the outside of the virus)—the part of the virus that triggers immune systems to develop antibodies to keep us safe. Dr. Corbett explains, "The cool thing [about mRNA technology] is you don't even need the lab to design the vaccine. All you need are the letters, or **sequence**, that **encodes** the virus's genetic material, on your computer screen."

Once they identified the part of the genetic sequence that represents the spike protein, it was time to figure out the best way to send that information, via a vaccine, to people's immune systems.

The Spike Through the Lens

"The SARS-CoV-2 virus is 1,000 times tinier than the width of a human hair," says Dr. Jason McLellan, professor of molecular biosciences at University of Texas at Austin. "A **cryo-electron microscope** let us look at the virus at that scale and create a detailed map of the [spike] protein."

The problem? "The spike protein is tricky," says Dr. McLellan. "Sometimes it looks like a baseball bat and other times, a spade. We needed to help the body recognize the most dangerous version—the spade shape." Dr. McLellan and his team tweaked the spike protein's genetic code, replacing two of its **amino acids** with sturdier ones to lock it in the spade shape.

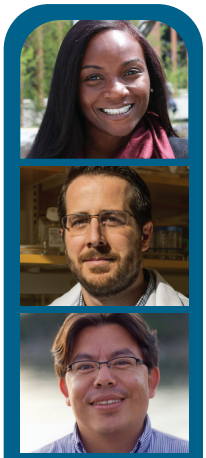
Dr. Corbett's findings on the genetic sequence of the SARS-CoV-2 virus and Dr. McLellan's procedure for stabilizing the spike protein are two examples of how scientists built on decades of existing research to develop the mRNA vaccines against COVID-19. Once the vaccines were created, they had to be thoroughly tested. Scientists use **clinical trials** to collect data on how well vaccines work. Most advanced clinical trials involve fewer than 3,000 volunteers and require a year to get the necessary data. In contrast, advanced clinical trials for COVID-19 vaccines enrolled more than 30,000 volunteers each—ten times more people! This allowed researchers to analyze sufficient data on the safety and efficacy of the vaccines in under four months.

"The SARS-CoV-2 virus is 1,000 times tinier than the width of a human hair."

Seeing Into the Future

Data can help address pandemics in many ways. Dr. Mauricio Santillana, director of the Machine Intelligence Research Lab at Boston Children's Hospital, predicts the future—not with a crystal ball, but with **machine learning** and mathematical modeling. His team uses data to make evidence-based predictions. Dr. Santillana explains, "If many people are searching for 'cough syrup' or 'symptoms of COVID-19' today, it may signal a problem." Coupled with mobility data (think: lots of people headed to a concert), Dr. Santillana can predict an outbreak weeks before it occurs.

"We share our findings with governors and health officials to help them make informed decisions, to help save lives."



From top: Dr. Kizzmekia Corbett, Dr. Jason McLellan, and Dr. Mauricio Santillana

Find definitions of bolded words on the bonus vocabulary sheet.

A MESSAGE FROM

VICE PRESIDENT KAMALA HARRIS

Science Is for Everybody!

When I was a child, my sister, Maya, and I used to go to our mother's lab. She was a breast cancer researcher—and she would give us jobs to do, like cleaning test tubes. When you are the daughter of a scientist, science has a way of shaping the way you think. For our mother, the scientific method was a way of life. And she would tell us about all the scientists she had worked with over her career—their many backgrounds, interests, and skills.

My mother believed in the power of scientific collaboration. Over the last two years, our nation has seen that power in action. To create the COVID-19 vaccines, all types of scientists came together to save countless lives. No matter who you are or what you are interested in, there are many ways to build a career in science.

- Do you like **solving mysteries**? You could be a **researcher**, uncovering how biological, chemical, social, and physical processes work.
- Do you like **drawing or coding**? You could be a **molecular animator**, creating 3D models of microscopic specimens and processes to visualize the results of experiments.
- Do you like **working with numbers**? You could be a **data scientist**, searching for important trends and insights in large amounts of data.
- Do you like **writing or speaking**? You could specialize in **public health communication**, helping to educate Americans.

The scientists who worked on the COVID-19 vaccines were once students just like you. One day, our nation might need your help to stop the spread of disease, invent life-changing new technology, or teach the next generation of scientists. So pursue your passions. And remember: Science is for everybody.

Scientists in the Spotlight

There are so many ways to be a scientist! Meet two top scientists with two different paths.

Erin A. Mordecai, Ph.D.

Associate Professor in Biology and Senior Fellow at the Woods Institute for the Environment, Stanford University

WANTS TO FIND OUT: how human impacts on the environment affect infectious diseases

What might surprise students about being a researcher?
It's not all about test tubes in the lab! One researcher might analyze mobile phone data to understand human mobility and contact patterns, where another might study satellite imagery of changing forest cover in the Amazon.

Wait, the Amazon rainforest? What does that have to do with infectious disease?
There are links between our impacts on the environment and our health. For example, climate change is making mosquitoes more capable of transmitting diseases in places where they couldn't before. Simultaneously, progress on malaria eradication is stalled by deforestation and destructive mining practices (which produce large areas of stagnant water, creating breeding grounds for disease-carrying mosquitoes).

Marcos J. Ramos-Benítez, Ph.D.

NIGMS Postdoctoral Research Associate Training Fellow, National Institutes of Health; Founder and President at Ciencia en Tus Manos, Inc.

WANTS TO FIND OUT: how the human body interacts with viruses during an infection

How do you hope your research will help people?
During an infection, human cells undergo changes. Though small, they really add up—resulting in severe illness. I study the small changes with the aim to discover targets for new treatments. I am proud to be part of a team that has tested a new drug for the treatment of severe COVID-19 infection.

What role does science communication play in your work?
As a Hispanic first-generation scientist, I founded Ciencia en Tus Manos, Inc. (translated: Science in Your Hands), a nonprofit dedicated to scientific communication for the Hispanic community, using language that's entertaining and easy to understand. Throughout the COVID-19 pandemic, I've seen directly how science communication saves lives.

Photos: Dr. Erin Mordecai, courtesy of Stanford University; Dr. Marcos Ramos-Benítez, courtesy of Dr. Ramos-Benítez

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