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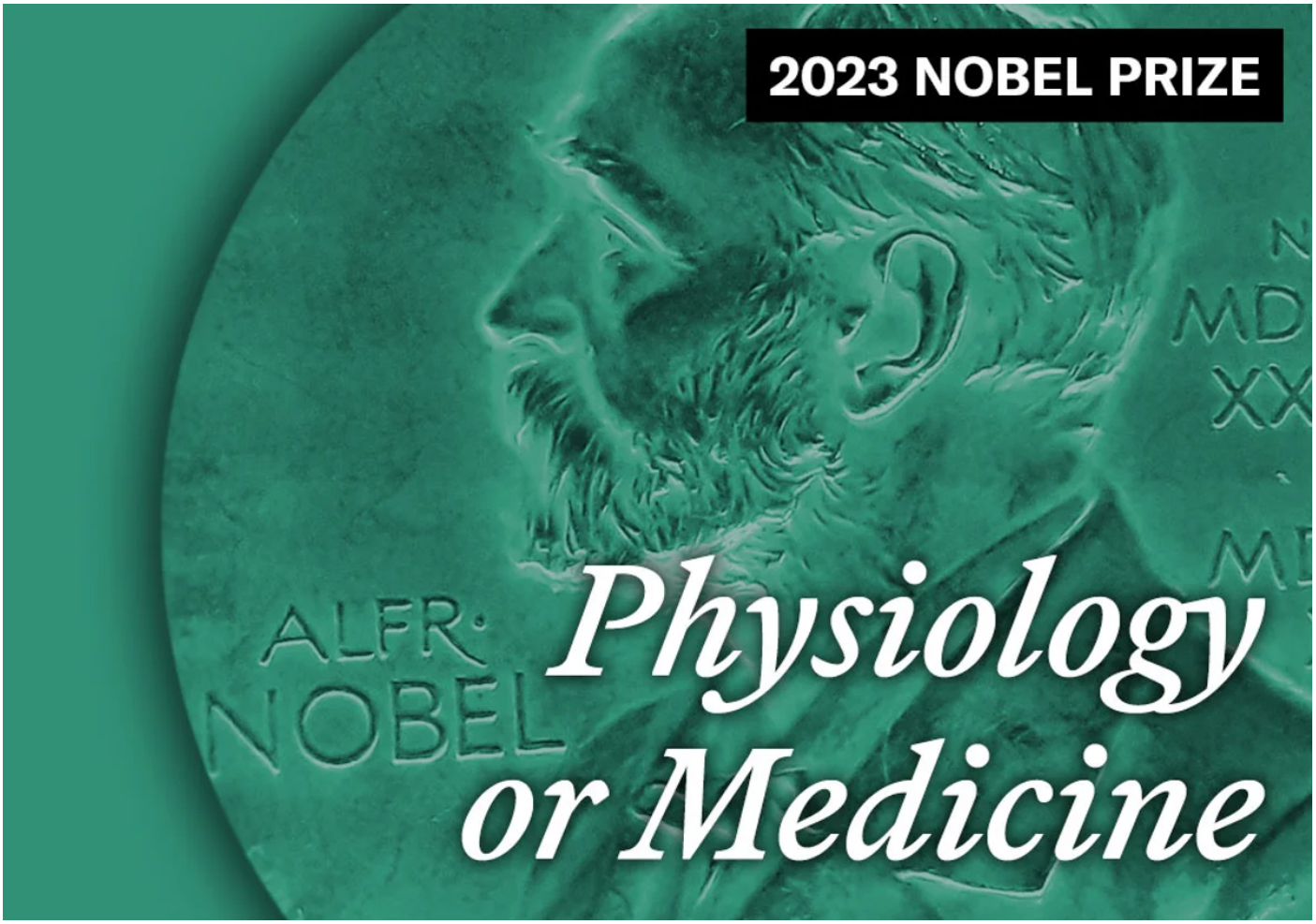
Scientists behind mRNA COVID Vaccines Win 2023 Nobel Prize in Physiology or Medicine

Katalin Karikó and Drew Weissman were awarded this year's Nobel Prize in Physiology or Medicine for mRNA vaccine discoveries that made highly effective COVID vaccines possible

BY LAUREN J. YOUNG EDITED BY JEANNA BRYNER



vanbeets/Getty Images (*medal*)

Vaccines

This year's Nobel Prize in Physiology or Medicine goes to a transformative medical technology that significantly altered the path of the pandemic and saved millions: the mRNA vaccines against COVID. Katalin Karikó and Drew Weissman were jointly awarded the prize for advancements that have changed the field of vaccine development and researchers' understanding of how messenger RNA (mRNA) interacts with the body's immune system.

Speaking to *Scientific American,* Weissman describes the rollercoaster of emotions he went through after learning of the news this morning. "I'm going through a series of steps, it started off just incredible enjoyment and surprise," he says. "And right now I'm pretty much numb."

Karikó and Weissman began studying in vitro synthetic mRNA technology in the 1990s, when they worked together at the University of Pennsylvania. The pair's seminal paper in 2005 described how they were able to successfully deliver modified mRNA into the body and trigger an immune response—the kind that trains the immune system for future viral infections. Over the years, their research with mRNA vaccines solved some of the major issues confronting the technique, such as the inflammatory response by the body that involves the production of harmful cytokines. During the pandemic, this mRNA technology led to the production of highly effective vaccines against SARS-CoV-2, the COVID-causing virus, and particularly ones that were adaptable for large-scale rollout.

"What's important here I think is that vaccines could be developed so fast," said Gunilla Karlsson Hedestam, a member of the 2023 Nobel Committee for Physiology or Medicine, at this morning's announcement. This was "largely due to ... improvements in the technology and this basic discovery."

Karikó was born in 1955 in Szolnok, Hungary. In 1989 she became an assistant professor at the University of Pennsylvania, where she remained until 2013. She was a senior vice president at BioNTech RNA Pharmaceuticals—a major manufacturer of an mRNA COVID vaccine—and is now an external consultant for BioNTech. She is also a professor at the University of Szeged in Hungary and an adjunct professor at the Perelman School of Medicine at the University of Pennsylvania.

Weissman was born in 1959 in Lexington, Mass. In 1997 he established his research group at the Perelman School of Medicine. Weissman is Roberts Family Professor in Vaccine Research at the University of Pennsylvania and director of the Penn Institute for RNA Innovation.

"The award, to me, is really a victory for vaccines and the potential for vaccines to advance health and improve equity," says Kathleen Neuzil, a vaccinology professor and director of the Center for Vaccine Development and Global Health at the University of Maryland School of Medicine.

Many vaccines had been created with weakened or deactivated whole viruses, but in recent decades many researchers have been investigating smaller viral parts, such as viral genetic material: DNA or RNA. When Karikó and Weissman injected the foreign in vitro mRNA into human cells, they found that it created a strong immune reaction that elevated protective antibodies. Subsequent inflammation, as well as enzymes in human blood and cells, would degrade the mRNA, however. Despite these scientific roadblocks, skepticism and difficulties with funding, Karikó and Weissman continued to search for solutions.

"It was nonstop technical hurdles for 25 years," Weissman reflects. "We couldn't get funding, Kati [Karikó] kept getting demoted and pushed out. It was very difficult to do this research, but we saw early on the potential and how important RNA was likely to be. And that kept us going. We never gave up."

The team found a way to modify mRNA to be less inflammatory—replacing uridine, one of its building block molecules, with a similar molecule called pseudouridine. They also developed a more efficient delivery system that used lipid nanoparticles to protect the mRNA and help it to enter cells for protein production.

"In the early days of vaccinology, we would take a bacteria, we would take a virus, and we would weaken it, or we would combine it with another antigen. But here this was really a targeted immune system approach, both from the use of the mRNA and the use of the lipid nanoparticle," Neuzil says. "So, to me, that was quite impressive—that they took an entirely different approach to vaccine delivery."

Starting in the early 2000s, Karikó and Weissman conducted several animal trials with mRNA vaccines for a variety of different pathogens such as Zika, influenza and HIV. “In every animal model we looked at, HIV was the only one that didn’t work well,” Weissman says. “Just about every single one of them gave us 100 percent protection.”

The research unlocked a new path for possible therapy and vaccine development—one that would prove critical during the COVID pandemic.

Adapting for a Global Public Health Emergency

When SARS-CoV-2 began to spread worldwide, Weissman and Karikó’s mRNA research quickly became a candidate and basis for vaccines against the virus. The mRNA vaccine approach had several advantages, Weissman explains. Only a sequence of the original pathogen was needed rather than an actual piece or full virus. “There’s no growing a virus and inactivating it. It’s a very simple procedure, and that’s because it’s a simple enzymatic reaction,” Weissman says. “It was two months from the sequence being released to the first patients getting the vaccine.”

Clinical trials, production and rollout of the vaccines greatly expanded, with companies creating hundreds of millions of doses within a year. “Switching over to COVID, it was just a technical thing,” Karikó told *Scientific American* in a 2021 interview. “It was already ready.”

The mRNA COVID vaccines work by injecting the genetic material specifically for SARS-CoV-2's spike proteins—surface proteins on the virus that allow it to bind to healthy cells. Modified mRNA in the vaccine is taken by cells, which then decode it and produce those spike proteins so that the immune system can better identify and neutralize the real virus in the event of a future infection.

"We're coming off the worst pandemic in more than a century, and certainly these vaccines contributed to lives saved and to less morbidity," says Neuzil, who has also been working on mRNA vaccines for malaria. "I think an adaptation of this technology and mRNA vaccines could really be transformative, particularly for low- and middle-income countries, because of the adaptability and flexibility of the platform."

Future Therapies

For future vaccines, the application can be quite broad, Weissman says. When Karikó first became interested in mRNA research, she wasn't initially seeking to develop vaccines. "I was making this modification in the RNA because I always wanted to develop it for therapies," she told *Scientific American* in 2021.

While the mRNA technology has helped to tackle the COVID pandemic, a tremendous number of people will benefit from the technology, says Niek Sanders, a principal investigator at Ghent University's Laboratory of Gene Therapy in Belgium. "It can also be used to treat any disease that is due to a malfunctioning protein as it allows patients produce their own therapeutic proteins," Sanders says. "Nobel Prizes with such a high impact on society are rare and occur only once in 25 or 50 years."

Weissman, Karikó and other research groups are already trying to apply the technology to autoimmune diseases, cancers, food and environmental allergies, bacterial diseases and insect-borne diseases. In July Weissman and his colleagues published a paper in *Science* that showed they could deliver RNA gene-editing machinery directly to bone marrow stem cells. This could be key for treating diseases such as sickle cell anemia, in which stem cells are typically taken from an individual, cultured and treated, and then put back into the body. "Now we can give them an off-the-shelf injection of RNA and cure their disease, and that has applicability to thousands of other bone marrow diseases. And then you can expand that to liver, to lung, to brain, to every other organ therapeutics," Weissman says. "The potential is just enormous."

Weissman hopes that the mRNA treatment will be available to sickle cell anemia patients in a year and a half. He also has many mRNA clinical trials underway, including a phase 1 trial for the disease amyloidosis and vaccine trials for HIV, norovirus and malaria. Wiessman's team is also planning to start clinical trials soon on a pan-coronavirus mRNA vaccine, which could help prevent future coronavirus epidemics.

"The future is now," Weissman says. "These therapeutics are in people right now."

LAUREN J. YOUNG is associate editor for health and medicine at *Scientific American*. She has edited and written stories that tackle a wide range of subjects, including the COVID pandemic, emerging diseases, evolutionary biology and health inequities. Young has nearly a decade of newsroom and science journalism experience. Before joining *Scientific American* in 2023, she was an associate editor at *Popular Science* and a digital producer at public radio's *Science Friday*. She has appeared as a guest on radio shows, podcasts and stage events. Young has also spoken on panels for the Asian American Journalists Association, American Library Association, NOVA Science Studio and the New York Botanical Garden. Her work has appeared in *Scholastic MATH*, *School Library Journal*, *IEEE Spectrum*, Atlas Obscura and *Smithsonian Magazine*. Young studied biology at California Polytechnic State University, San Luis Obispo, before pursuing a master's at New York University's Science, Health & Environmental Reporting

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