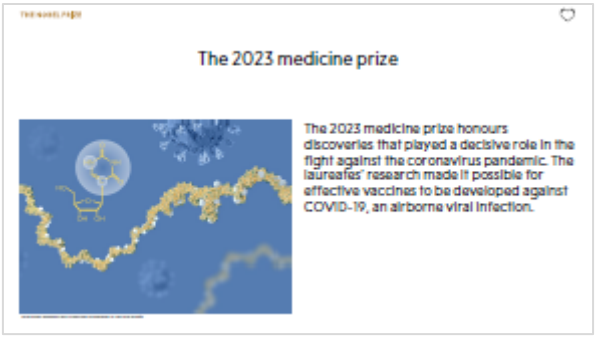
THE NOBEL PRIZE

Speaker's manuscript – 2023 medicine prize
Discoveries that laid the foundation for mRNA vaccines

The Nobel Prize in Physiology or Medicine

- The Nobel Prize in Physiology or Medicine is one of the five prizes founded by Alfred Nobel and awarded on 10 December every year.
- Before Alfred Nobel died on 10 December 1896, he wrote in his will that the largest part of his fortune should be placed in a fund. The yearly interest on this fund would pay for a prize given to "those who, during the preceding year, shall have conferred the greatest benefit to humankind."
- The Nobel Prize in Physiology or Medicine is thus awarded to people who have either made a discovery about how organisms work or have helped find a cure for a disease.

The 2023 medicine prize



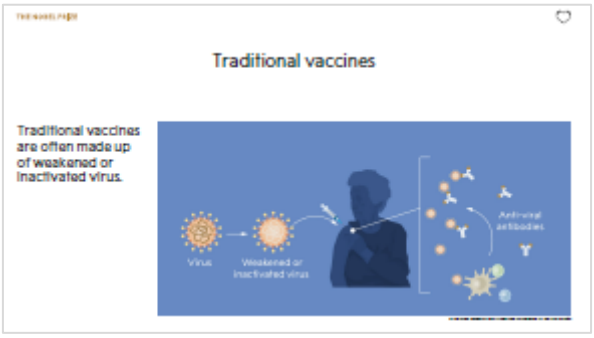
- The 2023 medicine laureates are being recognised for discoveries that were critical in the development of effective mRNA vaccines for COVID-19. The COVID-19 pandemic struck the world in early 2020.
- The laureates' ground-breaking research has fundamentally changed our understanding of how mRNA interacts with the immune system. Their work contributed to the extraordinarily rapid development of new vaccines during one of the worst health crises of our time.

2023 medicine laureates

- Katalin Karikó is a biochemist and has been working with mRNA for a long time. She was born in Hungary and later emigrated to the United States.

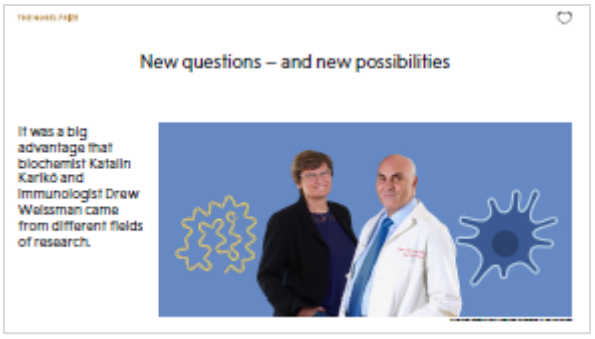
- Drew Weissman is an American immunologist who has long been interested in dendritic cells, which are an important part of the immune system.
- In the 1990s, while they were both working at the University of Pennsylvania in the United States, the two began a collaboration that increasingly came to focus on how mRNA could be used in medicine.

Traditional vaccines



- Vaccination stimulates the immune system to fight off foreign infectious agents, or pathogens, that enter the body. This process results in the formation of memory cells. These can quickly be activated and mass-produced by the body the next time it is exposed to the same pathogen. That protects the body against disease.
- Vaccines based on weakened or inactivated virus have been around for a long time. Examples include the vaccines against polio, measles and yellow fever. In 1951, Max Theiler was awarded the Nobel Prize in Physiology or Medicine for the development of a vaccine against yellow fever.
- In the last thirty years, methods have been developed for producing vaccines that only need to include certain parts of the virus rather than the entire virus.
- Vaccines that are based on weakened virus or parts of a virus stimulate the body's immune system. The next time the body is exposed to the virus, it is prepared and can fight off the virus effectively. Producing these kinds of vaccines is both time-consuming and expensive because it requires large-scale cultivation of cells. That makes it hard to adapt the vaccine to mutations of the virus and to produce it quickly enough for use in a pandemic.

New questions – and new possibilities



- In searching for alternatives to traditional vaccines, researchers long tried to develop new vaccine technologies that didn't rely on large-scale cultivation of cells.
- Inside our cells, the genetic information in DNA is transferred to messenger RNA, also known as mRNA, which serves as a template for the production of proteins. During the 1980s, efficient methods were developed for producing mRNA without cultivating cells, known as *in vitro*-transcribed mRNA.
- This spurred the use of mRNA in vaccines, but barriers remained that limited its widespread use. In addition to the fact that mRNA is unstable and difficult to transport in cells, it turned out that mRNA produced in a laboratory (*in vitro*) caused inflammatory responses.
- These obstacles did not discourage Katalin Karikó, who had long dreamed of using mRNA to treat and cure diseases.

- During the same time period, Drew Weissman was working with dendritic cells, which play an active role in the body's immune system. In the borderland between their two fields of research, new questions emerged – but also new opportunities.

The breakthrough

- Katalin Karikó and Drew Weissman noticed that the body's cells reacted to *in vitro*-transcribed mRNA in the same way they reacted to mRNA from bacteria. That caused a reaction that produced inflammation in the body.
- The researchers wanted to understand why mRNA made in a laboratory stimulated the body's immune system, but mRNA taken from the cells of mammals did not.
- They tested making small modifications to the different nitrogenous bases (A, U, G and C), or nucleosides, that are the building blocks of mRNA. They discovered that when they modified the nucleoside U on the atomic level, there was no inflammatory response. It also increased the production of proteins by the cell's ribosomes.
- Through these discoveries, Karikó and Weissman broke through the barriers to using mRNA in the production of new medicines.
- They carried out this work during the early 2000s.

Outbreak of the coronavirus pandemic

- Interest in mRNA technology began to take off, and by 2010 there were already several companies working with it.
- In response to the outbreak of the coronavirus pandemic in early 2020, because the technology was already established, two base-modified mRNA vaccines could be produced at record-breaking speed.
- One of the things that is specific to a coronavirus is the so-called spike proteins that sit on its surface. Researchers at pharmaceutical companies used mRNA technology to create a vaccine that holds the virus's recipe for producing these spike proteins. The ribosomes in the body's cells then manufacture spike proteins according to the recipe. The proteins attach to the surface of the cell, and the body's immune system reacts to them, forming memory cells. If a vaccinated person is later exposed to the coronavirus, their body is already prepared and can more easily fight off the virus.
- These vaccines were shown to be about 95% effective.

For the greatest benefit to humankind

- Several other kinds of vaccines for the coronavirus were developed quickly, and in all more than 13 million vaccine doses have been given around the world. These vaccines have helped make it possible to save the lives of millions of people while inhibiting the spread of the disease and easing its symptoms.
- The superior flexibility and speed with which mRNA vaccines can now be manufactured is paving the way for the development of vaccines for other infectious diseases as well.
- In the future, mRNA technology can also be used in the treatment of certain forms of cancer.

"As important as the vaccine is, if you don't take it, it doesn't work!"

- In an interview given in conjunction with the announcement of the 2023 medicine prize, Drew Weissman speaks about his and Katalin Karikó's research, which made possible the development of effective vaccines for COVID-19.
- When asked if he believes that the Nobel Prize will help combat vaccine hesitancy, Weissman responded that for people who are sceptical but still believe in science, the Nobel Prize could make a difference.