Resilience, scepticism, and mRNA

The story of Katalin Karikó

The COVID-19 pandemic presented the world's governments and health organisations with a vaccination challenge on a scale it had never experienced before. Messenger RNA (mRNA) vaccines were critical in the production and distribution of affordable vaccines across the globe. Katalin Karikó's 40 years of research into mRNA was the cornerstone of what made this possible. In this interview, we find out more about her incredible life and career.

Born in 1955 in rural Hungary, Katalin Karikó battled critics and scepticism for her research into messenger RNA (mRNA) for over 30 years before its role in the COVID-19 vaccination programme gained her recognition and, in 2023, a Nobel Prize in Physiology or Medicine. After her move to the United States in 1985, Karikó was labelled by colleagues as 'that crazy mRNA lady', and her team head at Temple University even attempted to have Karikó deported to stop her taking a job at Johns Hopkins University. Despite all this, she remained firm in her belief that her research was important and valuable. In this interview, Karikó tells *Research Outreach* why she loves biochemistry, what it's like to win a Nobel Prize, and how she would advise young scientists today.

Katalin Karikó, 2023 Nobel Prize laureate in Physiology or Medicine.

What is your educational background and how did you become interested in biochemistry?

I grew up in a small town, so nobody was a biochemist around me, but I was interested in nature and wanted to understand. I had great teachers. I was accepted at a university and I ended up in biochemistry by chance. I am not a visionary and don't have special talents or super memory. I was curious, and then I put my time in and took whatever opportunity was given to me to make the best out of it.

Can you tell us about your collaboration with Drew Weissman and the key breakthroughs and lessons that you learned when working together?

I started to work with messenger RNA in 1989 when I worked at the University of Pennsylvania, and I had already been working for almost ten years when I met Drew at the Xerox machine – at that time, we copied articles if we wanted to read them. We started to chat; Drew was trying to develop an HIV vaccine and I told him that I was working with mRNA and that's how it started. It's important for researchers or colleagues in any organisation to meet each other and talk about what they are doing! He wanted to test whether messenger RNA would be good for vaccines.

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He used a very special human cell type and we realised that when we delivered messenger RNA that it responded with inflammation and nobody could understand why it was inflammatory. We were curious to understand, and that's how we discovered that we could make the RNA non-inflammatory. We set out to make non-immunogenic mRNA. We didn't even know that existed, but that's what science is all about.

Is open curiosity the general attitude that you take towards teaching?

I think that is important. Let the child or the young one be curious; show them how to find the answer for their questions and present them with even more challenging things and then you know they can get engaged. I also think it's very important to let them experiment with their own hands; just a simple thing like picking up leaves from a tree and then looking at them against the sun.

What was it like to win the Nobel Prize?

I have to mention that for 40 years of my work I never got any award, not even a grant and I was fine with that. I did not need any university authority to tell me I was doing a good thing. I knew it. Four years ago I got the first award and for days I couldn't comprehend that. People say, 'oh, every scientist dreams of getting the Nobel Prize' but I was never one of them. It is the greatest honour but some people might have been happier that I received the award. For me, the letters I received from people who were

Karikó's book 'Breaking Through: My Life in Science' has been translated into ten languages and serves as an inspiration to those curious about science worldwide.

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grateful is more touching. To know that I was part of a process that helped others; that feeling was so much more valuable for me.

At the beginning I was wondering what I should say when they had a microphone in front of me; in 40 years in a laboratory, you don't have to give interviews, especially if you are a scientist who works at the bench. When a prize is given, the spotlight is on the scientist and I realised that the public understanding of what a scientist is doing is important. We had neglected that, so every time I gave an interview we needed to educate the public. I also thought that it was important for the upcoming generation to realise that science is an exciting thing, it's a passion. My work shouldn't portray that I am suffering because I went to work on the weekend; I wanted to be there because I had an idea that I wanted to try out. I had fun. Finally, when I receive an award I always acknowledge all of my fellow scientists' work because we all work together, research is a team sport.

Over your 40 years of work, how has the field changed?

When I started to work in 1989, we were happy that we could generate messenger RNA. Then we put in cells that could detect that messenger RNA translated to a protein. Thirty years later there are more than 250 clinical trials ongoing using messenger RNA for many different vaccinations for viruses, bacteria or parasites. There are gene therapies ongoing as well.

The major advantage of mRNA is that it can be very quickly and cheaply made. Even if the final product is a protein, with the screening and everything else on mRNA, the messenger level is much faster, and you can make the product more cheaply. Eventually if the mRNA is delivered to the body, the patient will generate the product which has the biological activity, the drug, and that is much better (and cheaper again). Many of the drugs which are right now unaffordable as a protein we deliver at mRNA level in a way that would be affordable for many, many people. It is important for me that it is not million-dollar therapy.

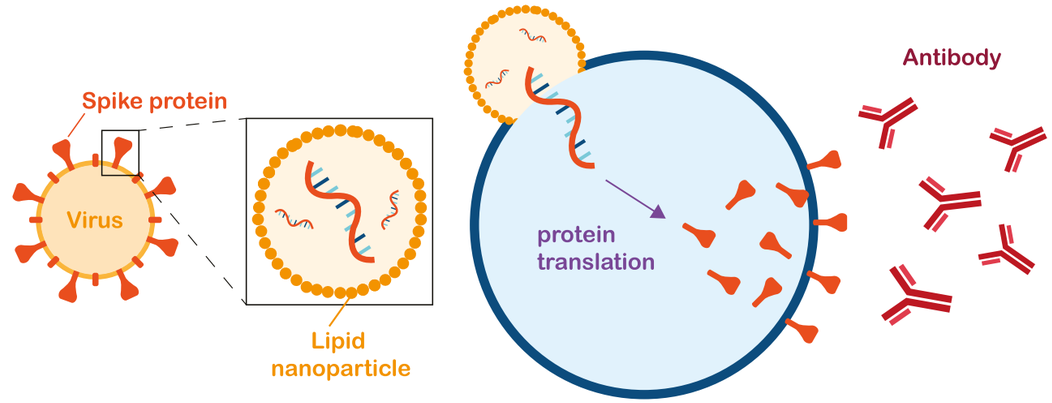
We didn't even want to patent our work, because we wanted everybody to use it, but we were told that nobody would use it then! Nobody will test it because when they do a clinical trial and make that investment, they would know there is no patent to protect that investment.

Have you found it difficult to deal with people that are sceptical of ideas throughout your career?

I have to say that scientists are always sceptical. They don't believe, they want to prove it and that's why they do the next experiment. Advancement in science happens because sceptical scientists point out shortages and then other scientists try to prove this way or that way. There are also people, venture capitalists, who can invest and they are risking money where there is no guarantee, so I think it's natural how they act.

What was it like to communicate ideas, particularly ideas around COVID-19, that people are quite sensitive about?

I realised that a product which is FDA approved is not necessarily accepted by the public. We needed public understanding and then acceptance by the public that the drug was developed safely. Somebody had to explain that messenger RNA, which is in this vaccine, is not something that we invented, nature invented it. I had to explain that the virus itself has messenger RNA, but it had many many other genes which can make you sick and we just selected one little piece of it which can help to educate your immune system to recognise when you get infected. But



Throughout her lifelong studies of mRNA in pursuit of affordable vaccines, Karikó has faced and remained resilient to considerable challenges.

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the biology is complex. We have to find words to explain this to the public.

During COVID-19 I realised that we had not done enough, and many people simply didn't understand what was happening. Scary things were circulated on social media: that mRNA would change your genome, or two years from now everybody will drop dead, or you'll never have children and so on.

Is there any advice you might give to up-and-coming scientists?

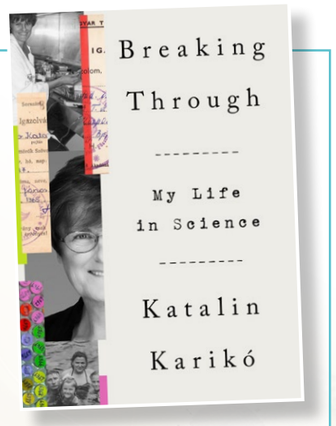
For the next generation, I would tell them that the most important thing is that they enjoy what they are doing. If they like to solve puzzles, science and research might be good for them. The feeling that something you did may help to cure a disease across the globe, even if you don't see the outcome directly, is what science is all about; to be a scientist is exciting. My daughter was a rower. Rowers go backwards, and I used to tell her that it is like science. We may not see the finish line or even know that we are going in the right direction, but we are pulling like rowers do.

I would also say that physical and mental health is important for everybody. They won't be able to proceed unless they are physically and mentally healthy. I was always exercising, swimming, and running. I even ran a marathon just to test myself, to see if I could last for 42 kilometres.

Mentally, I was helped by understanding how to handle stress. At age 16 I read Hans Selye's book (a Hungarian who immigrated to Canada, and coined the word 'stress'). He described how stress can kill somebody but that it is not the stress itself that kills, it is how the person perceives it. He also mentioned that you need positive stress like expectation and excitement. You have to convert the negative stress to a positive one. The great Roman philosopher, Marcus Aurelius, also held that you have to focus on what you can change, rather than things out of your control, to guide you in life.

Katalin's book Breaking Through: My Life in Science is now available to read in English, as well as several other languages.

Interview conducted by Todd Beanlands
todd@researchoutreach.org



Further reading

Read Katalin's book: Breaking Through: My Life in Science