

mRNA Discovery: Who Wants the Prize?

- The mRNA vaccines are the main weapon in the fight against the pandemic - but who really invented them?
- The researchers argue about this themselves.
- It's also about who actually deserves the Nobel Prize now.

The serenity that Robert Malone exudes in this video interview on a June morning during the American East Coast: It is definitely deceptive. With his gray, thick beard, narrow eyes and firm voice, the 61-year-old looks like someone who can only be shaken by little. But the story he tells at his home in Madison, Virginia is about pain and disappointment. "It feels," he says, "like a rape."

What Malone means is the feeling of having discovered and described something - perhaps the first, or at least one of the first - and then seeing others who came later and built on it are celebrated and praised. "And that's really painful."

Robert Malone has decided to be radically open, also with regard to himself. A kind of self-therapeutic honesty, as a result of great hurt, that's how it works.

The proof of feasibility

The story he is interested in goes back more than 30 years. In the late 1980s, Malone is a young, fervently ambitious scientist, a PhD student at the Salk Institute in California, a research facility founded by Jonas Salk, the developer of the polio vaccine. Like many researchers of this time, he was inspired by the belief in gene therapy, in the possibility of defeating the great diseases of mankind by interfering with the genome. In 1989 he co-authored and drove a scientific article describing how messenger RNA wrapped in fat globules induces cultured cells to produce certain proteins.

It is the first scientific description of the main features of the technology that is today in the process of saving countless lives and showing mankind a way out of the pandemic: the mRNA vaccines. A "proof of principle", as it is called in science: the proof of feasibility.

Malone is unknown outside of the specialist world

"Robert Malone was the first to describe this principle and thus described the basis for the development of mRNA vaccines," says immunologist Jan Dörrie, specialist in RNA-based immunotherapy at the University Hospital Erlangen. And yet Robert Malone is hardly known to anyone outside the world of scientific specialists.

Can that be fair? And who does the fame for this technology go to, which might just redeem the world? Or at least that part of the world that can afford this form of salvation?

Nobel Prize is within your grasp

In any case, barely a year and a half after the pandemic began, the fight for fame is in full swing. A fight about money, recognition and prizes. It seems clear in June 2021 that it is the mRNA vaccines in particular that are making the greatest contribution to taking the horror of the coronavirus.

They are all based on the same principle: They contain a messenger RNA, i.e. the blueprint for certain virus fragments, against which the body then forms antibodies. The vaccines from Biontech / Pfizer and Moderna are based on it. According to all studies, these agents are highly effective, quickly produced in large quantities and, on top of that, easily adaptable to new mutants - all advantages that should also occupy the Nobel Prize Committee before the announcement in October. The theme of the award has seldom been as close as this year.

Only: who deserved the grand prize? And does science actually still work today in such a way that in the end one or a maximum of three people can celebrate? Is science still so much a loner?

Katalin Karikó is considered an inventor in the USA

There is already an answer to this in the USA. There, Katalin Karikó is known as the "mother of the mRNA vaccine". The Hungarian moved to the USA with her family in 1985, has been researching mRNA since the early 1990s - and in 2008, together with her colleague Drew Weissman, described a modification thanks to which the mRNA undermines the immune defense of the cells and is not destroyed so quickly.

Karikó sold her car to emigrate to the USA, and she and her husband hid the savings in their two-year-old daughter's teddy bear - she told the Guardian. It is a story in the style of the American dream embodied by the 66-year-old. Karikó is a researcher at the University of Pennsylvania. The Mainz company Biontech of the German-Turkish vaccine developer Ugur Sahin has secured its services, there she holds a position as Vice President.

Karikó recognizes the merit of his colleagues

In television interviews, as most recently with CNN, Karikó looks as if she would rather retreat to her laboratory and continue researching immediately. But when it comes to awarding the

Nobel Prize, she can count on important advocates. If you ever asked him, said Derek Rossi, co-founder of the pharmaceutical company Moderna, "I would put you right in the middle".

In the opinion of many research colleagues, it belongs there, in the first row. Just not alone. She sees it that way too. "I have," she wrote in an email to Robert Malone at the beginning of June, "many reporters about you, Ingmar (Hoerr, co-founder of Curevac), Ugur Sahin (co-founder of Biontech), Stephane Bancel (Moderna) and all the others Sent scientists in this field. "

Your reference tells of the honest attempt to point out the complicated and long history of the origins of mRNA vaccines. It is an attempt that it is not clear whether everyone always makes it with the same verve.

A historical mistake

"The man who reinvented vaccination" is the rather immodest title of a biography about Curevac co-founder Ingmar Hoerr, which has just been published by Aufbau-Verlag. It tells the tragic story of Hoerr: In March 2020, at the beginning of the pandemic, he suffered a stroke and fell into a coma for weeks. Then he had to fight his way back to life - and later see how Curevac lost the race for the first vaccine. To date, the Tübingen-based company does not have all the data required for approval.

Hoerr's scientific achievements are beyond any doubt. He is also a Nobel Prize candidate. Together with other Tübingen researchers, he was able to stabilize the mRNA, whose rapid decay had been the main problem, inoculating the first people with mRNA, founded a company and laid the foundations for mass production.

The starting point for him at the end of the 1990s was a central finding: that an immune reaction can be generated in mice using mRNA, originally a coincidence. "It was then that I realized that I had discovered a fundamental principle: You can vaccinate with mRNA," said Hoerr in May of "Die Zeit".

Previous basics as a basis

But was he really the first? At that time, "it became clear to him that there is a practicable way of actually using RNA as a vaccine on humans," explains Hoerr today when asked.

His discovery was "naturally embedded in the context of the current state of science". Others would have provided important scientific foundations without which his work "would not have been possible in this form," Hoerr mentions among others, Robert Malone. For the researchers before him, however, it was not about the application in humans, but about basic research.

Another pioneer: Peter Liljeström

But others had come a long way in this field - the French Pierre Meulien and Frédéric Martinon, for example, but also Peter Liljeström. In 1994, the scientist from the Karolinska Institute in Stockholm described how he vaccinated mice against influenza in this way and observed a strong, sustained immune response. And whoever calls the now 68-year-old, who was head of the vaccination department of the Swedish epidemic authority for more than 16 years, learns that the actual experiments took place much earlier. "1988", says Liljeström. Originally, he hadn't even planned to publish the results at all - and only did so when he noticed the growing interest in the topic.

Nevertheless, Liljeström seems free of bitterness. "I am very pleased that the mRNA vaccines are being used so successfully today," he says. "And that we could make a contribution to it." At that time, he too tried to develop this technology further, but he couldn't find any sponsors. The industry waved it off. "MRNA was considered too risky," says Liljeström. Too unstable, too unreliable, nothing for the future. A historical mistake.

Against all odds

The question of who the first one was can hardly be clarified. "At that time, a lot of people were doing research on the topic at the same time; we were driven by the same questions," says Liljeström. What they described at the time was the principle of the vaccinations that are used today. "But we were just too early."

But who does the credit for these vaccines go to? The ones who came up with the original idea? Or those who, against all odds, pursued this idea to the end, which ultimately made the production of the vaccines possible? Which they optimized for use in humans?

Andreas Radbruch, immunologist and scientific director of the German Rheumatism Research Center Berlin, counts the work of Hoerr, Karikó and Biontech founder Sahin as one of the decisive steps - and that of Peter Liljeström. It is difficult to say who will actually receive a Nobel Prize - "but in fairness Liljeström would have to be there".

"In no case would it be appropriate to separate development from those who gave the original impetus," says Erlangen-based immunologist Dörrie.

The search for origins seems endless

"35 years, hundreds of scientists, countless companies, and billions of dollars have led to today's mRNA vaccination," said Philip Felgner, director of the Vaccine Center at the University of California Irvine. "The thanks can be distributed over a large area." Whereby the origin of the research is in 1984 - the year when those nanoparticles were discovered in his laboratory at the Syntex Institute in Palo Alto, in which genes can be smuggled into cells. A technique that today's vaccines also use.

It's like asking about the origins of vaccines rarely ever comes to an end, like there's still one more lead.

One of the rules of the Nobel Prize is that a maximum of three scientists per category may be awarded. That could become a big problem in this case, and perhaps an obstacle to trying to award the prize for this discovery in the first place.

Malone wants a fair tribute

Incidentally, Robert Malone, the author of the first article, never worked on the subject again. At that time he moved to another institute - and left there after three months due to personal differences. The patents, however, remained with the institute, which then resold them without anyone pursuing them.

Malone has continued to work as a scientist and consultant, on other issues. What remains, however, is its sensitivity if someone's contribution to these vaccines is suppressed. His research was only possible thanks to other forerunners, he emphasizes. It is not about himself, but about a fair appreciation. "We all stand on the shoulders of giants," he says, following an old Newton quote. This seems to be particularly true in the case of mRNA vaccines.