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Breaking Through Barriers: Meet the Minds Behind Emerging mRNA Technology

Announcer:
You're listening to *Medical Breakthroughs from Penn Medicine*, advancing medicine through precision diagnostics and novel therapies. Here's your host, Dr. John Russell.

Dr. Russell:
After joining the University of Pennsylvania in 1998 as an immunologist, Dr. Drew Weissman began exploring how mRNA technology could be harnessed to create a new kind of vaccine. And after stumbling upon fellow researcher Dr. Katalin Karikó at the office's copy machine, whose decades-long efforts to better understand mRNA technology brought her to the University of Pennsylvania, Dr. Weissman discovered a mutual interest in uncovering the clinical applications of mRNA technology. Together, the two researchers forged forward in their efforts to understand the potential clinical applications of mRNA, pioneering the mRNA technology that led to the development of the COVID-19 vaccines. But what's on the horizon for this novel technology? And how is the research reshaping both the landscape for vaccine development and the future of gene therapy?

Welcome to *Medical Breakthroughs from Penn Medicine* on ReachMD. I'm Dr. John Russell. And joining me today to take a deep dive into the future of mRNA technology are Dr. Drew Weissman and Dr. Katalin Karikó. Looking at each of their backgrounds, Dr. Weissman is a professor of medicine at the Perelman School of Medicine at the University of Pennsylvania. Dr. Weissman, welcome to the program.

Dr. Weissman:
Thank you very much for inviting me.

Dr. Russell:
And Dr. Karikó is a biochemist and adjunct professor at the Perelman School of Medicine at the University of Pennsylvania. Dr. Karikó, thanks for being here today.

Dr. Karikó:
Thank you very much for inviting me. I am happy to be here.

Dr. Russell:
So I'd love to start by congratulating you both on recently being named Time's 2021 Heroes of the Year, so well deserved, and receiving the Lasker-DeBakey Clinical Medical Research Award. With that in mind, Dr. Karikó, can you tell us what this recognition means for your future endeavors?

Dr. Karikó:
Of course, you know, the recognition is a wonderful thing. And I am deeply honored, and especially the privilege to belong to the group of scientists who were recognized similarly to that. And right now, I don't know that how it will change the future. I think that it will be the same, because for 40 years, I was very much enthusiastic and working very hard without any recognition. So, I don't think that it changed. It is very nice that it is recognized. But again, also I would mention that so many scientists contributed to this success, and so I usually just feel that I am one of the many, many scientists who is recognized, but all of them deserve recognition.

Dr. Russell:
So the same question for you, Dr. Weissman, how do you see these accolades impacting your future research efforts?

Dr. Weissman:
I completely agree with Katie. I'm highly honored to receive these awards. It's wonderful recognition. But we have to remember, it isn't just Katie and I. Many scientists were involved in discovering RNA, developing RNA. Many scientists were involved in making the vaccines. There's so much that's involved above and beyond what Katie and I did. I really feel everybody should share this honor. For my future, my future is going to continue as my past. I'm going to keep doing research. I'm going to keep investigating new things, developing new approaches and treatments with RNA.

Dr. Russell:
So, Dr. Weissman, accolades aside, is it going to be easier to fund mRNA research going forward with all of this recognition?

Dr. Weissman:
Yeah, I think the recognition of RNA as a great vaccine for COVID-19 will do a lot of things. It's going to allow the FDA to screen and analyze future vaccines much easier. It's certainly going to increase funding for mRNA vaccines, and that will have spillover into other vaccines. I don't think the accolades are going to particularly help with funding. I think they help with the recognition. But it's really the billion people that have received the vaccine that's going to increase its use, increase its recognition, and improve funding.

Dr. Russell:
Well, thank you both for sharing your emotions and sharing the accolades with so many other people who've worked with you along the way. Now, Dr. Karikó, if you take a look at mRNA technology in the context of the COVID-19 pandemic, how will it allow the vaccine to flex for new variants that might come along?

Dr. Karikó:
So far, it seemed that, we didn't need it a new vaccine for the different variants. But if, it seems that the original vaccine is not protective enough, then it is very easy to develop a new one and you are already aware that for the Omicron, there is already clinical trials running. And it's the same for other different viruses that developing a new vaccine against those will be much easier using this RNA technology.

Dr. Russell:
So Dr. Weissman, a related question for you. We hear about all these new variants. How does the mRNA technology allow researchers like yourself to be nimble in the face of new variants that might appear?

Dr. Weissman:
Yeah, so the RNA vaccine only requires a sequence. And once that's available, the vaccine can be made very quickly. It takes a couple months, two to three months to make a new vaccine for a variant. The problem is chasing variants because by the time you make a vaccine for the current variant, a new one is likely to appear.

Dr. Russell:
For those just tuning in, you're listening to *Medical Breakthroughs from Penn Medicine* on ReachMD. I'm Dr. John Russell, and today I'm speaking with Dr. Drew Weissman and Dr. Katalin Karikó, about mRNA vaccine technology.

Now, if we look ahead to the future, Dr. Karikó, where is mRNA technology research and its clinical applications headed when it comes to infectious disease such as HIV or Zika?

Dr. Karikó:
I mean, for the HIV and Zika and other viruses for the vaccine direction, maybe Drew Weissman, my colleague, can talk more. My original goal was always to develop messenger RNA that codes for therapeutic proteins and those are in a big field and it advanced very well in recent years. And, just many people were not aware of those messenger RNA were already in clinical trials. And people thought that maybe the vaccine is the first one but, other diseases clinical trials were already running with messenger RNA.

Dr. Russell:
So turning to Now, Dr. Weissman, is a potential application for autoimmune deficiencies or disorders such as sickle cell anemia?

Dr. Weissman:
RNA has enormous potential. It's a platform technology. You've already mentioned many of the vaccines. There are many other diseases that RNA is being developed for, including malaria, tuberculosis, hepatitis C, the list just goes on and on. But, as Katie just mentioned, there's a whole side of RNA for therapeutics, delivering monoclonal antibodies, delivering congenitally-deficient proteins. To me, the most exciting is the potential future of targeting RNA LNPs to cells in vivo, which may allow us to do in vivo gene therapy. For sickle cell, that's critical; 200,000 people a year are born with sickle cell in mainly in Africa in India. To take their bone marrow out to treat their disease is impossible. mRNA LNPs should allow in vivo gene therapy, where you give a single injection, the LNPs target the bone marrow stem cells and correct the genetic disorder. That would be game changing for the treatment of sickle cell and many other

genetic diseases.

Dr. Russell:
Wow. So my final question to you, Dr. Weissman, we all know the kind of impact mRNA technology has had in the battle against COVID-19. So, can you tell us how this technology might be used in future pandemics?

Dr. Weissman:
Yeah, I mean the thinking early on was that RNA would be the perfect vaccine for a pandemic. You don't need the virus, you only need the sequence. And once you've got the sequence, it can be made very quickly. The real thing with pandemics, though, is realizing when they begin. And that allows you to start very quickly. So, I think surveillance is critical for pandemics in the future. Once people can identify a new virus quickly, RNA can come in, you can make the vaccine. I heard Uğur Şahin say it would take them three months to make a vaccine against the new virus. So that's incredibly fast. And I think RNA with its efficacy and its speed is primely positioned for future pandemics.

Dr. Russell:
Well, with those forward-looking thoughts in mind, I want to thank my guests Dr. Drew Weissman and Dr. Katalin Karikó, for giving us a look into the future of mRNA technology. Dr. Weissman, Dr. Karikó, it was great speaking with you both today.

Dr. Karikó:
Thank you for the opportunity.

Dr. Weissman:
Thank you very much.

Announcer:
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