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Miracles in Medicine: Exploring the Past, Present, & Future of mRNA Vaccines

Announcer:
Welcome to *VacciNation* on ReachMD, sponsored by Moderna. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is *VacciNation* and I'm your host Dr. Jennifer Caudle and joining me to explore the past, the present, and the future of mRNA vaccines is Dr. Drew Weissman, Professor of Medicine at the Perelman School of Medicine at the University of Pennsylvania. Dr. Weissman has played a central role in the research, development, and advancement of mRNA vaccines, and is a recent recipient of the Lasker-DeBakey Clinical Medical Research Award honoring outstanding achievements in clinical medical research. Dr. Weissman, welcome to the program.

Dr. Weissman:
Thank you.

Dr. Caudle:
So, let's begin with some background, Dr. Weissman, what initially got you interesting in mRNA technology and what was your initial goal in digging into this therapeutic potential.

Dr. Weissman:
Well, I moved to the University of Pennsylvania in 1997 and my interest then was to make vaccines using dendritic cells. Dendritic cells are a highly specialized immune cell that starts immune reactions. So, it's the obvious target for a vaccine. When I got to Penn, I met Katalin Karikó, who had been studying mRNA therapeutics for a number of years. We got together and started working together and we made a bunch of observations that pushed us to the point of making RNA therapeutics and vaccines.

Dr. Caudle:
That's really exciting. And with that in mind, can you describe some of the steps that went into leveraging mRNA technology as vaccines?

Dr. Weissman:
So, there were a huge number of steps. The critical one that we addressed when we first started was we found that RNA was very inflammatory. So, what happened when we put it into a mouse, the mouse got sick and you obviously can't make a therapeutic that makes people sick. So, we spent seven years trying to figure out why RNA made animals sick. And that's when we figured out to change the nucleus side, so change one of the letters in the RNA into a modified version, and that got rid of the inflammation and started the new renaissance in RNA therapeutics in RNA vaccines.

Dr. Caudle:
And what about the collateral issue of scientific skepticism that must've followed mRNA vaccine technology early on; how did your team push past that?

Dr. Weissman:
So, Kati and I looking back on this we started working in '97 or so, we couldn't get grants, we couldn't get papers published, people just weren't interested in RNA. There had been previous work that went nowhere, so we were constantly confronted with skepticism. We thought when we published our modified RNA gets rid of inflammation that people would've changed their minds, but it took a lot of years before people finally changed their minds and started to work with mRNA. We just kept pushing through, I mean, we weren't dissuaded by the skepticism.

Dr. Caudle:
For those of you who are just tuning in, you're listening to *VacciNation* on ReachMD. I'm your host, Dr. Jennifer Caudle and today I'm speaking with Dr. Drew Weissman about the emergence and evolution of mRNA vaccines.

So, Dr. Weissman, let's review mRNA technology in the context of the global COVID-19 pandemic. You know, we know these vaccines weren't initially developed to combat a pandemic, so that must've been, you know, quite a turn of events to see them become our primary weapon against it. What can you tell us about this?

Dr. Weissman:
Certainly. I work in an infectious disease division, which is full of epidemiologists, who are people who study and predict new pandemics. So, in November of 2019, we started hearing about new pneumonia cases in Wuhan, China and we started to talk with each other, and we were concerned by the data. I have friends who worked at the Wuhan virologic institute who were telling me that it was worse than what the government was saying, which made us incredibly concerned. So, we were right on top of this before the sequence was released. The problem was we knew the modified RNA vaccine would be a great approach. We didn't know what the virus was. So, when that sequence was released in early January, we immediately made vaccines and started testing it in animals and pushing to clinical trials.

Dr. Caudle:
That's remarkable. And what was it about this particular technology that enabled us to pivot, as you mentioned towards addressing the COVID-19 pandemic so quickly?

Dr. Weissman:
Well, people have to understand that we have been studying modified RNA for 15 years. It wasn't brand new technology. It had already been in a couple of clinical trials, so we knew how to make it for people. We knew how to give it to people. and we knew what to expect. And we expected very good responses and very good protection and luckily, that's what we found.

Dr. Caudle:
Yeah. That's amazing. You know, if we look more broadly at mRNA technology, what do you see on the short term and longer term horizon in terms of ways this could be applied therapeutically?

Dr. Weissman:
So, we actually have five phase one clinical trials for things like influenza, HIV, genital herpes that we started before the pandemic hit. So, we're moving ahead with those clinical trials. We also have many more vaccines that we've developed for things like malaria, TB, hepatitis C, norovirus, and a bunch of other diseases that we're developing and pushing to do clinical trials on. So, I'd expect to see a huge number of vaccines going through clinical testing and ultimately receiving approval over the next few years. So, that's the short term.

The long term RNA has just a huge number of potential uses. We've developed what we call in vivo gene therapy and what that means, so the way you do gene therapy currently for sickle cell is you take bone marrow out of a patient, you infect it with a lentivirus that fixes the broken gene, and you give the bone marrow back. 200,000 people a year are born with sickle cell in sub-Saharan Africa, and you can't do 200,000 bone marrow biopsies and infections. So, we figured out how to target bone marrow stem cells with an IV injection of an mRNA LNPs. So, we can give a single IV injection and correct the genetic defect in sickle cell and cure the disease. I think that's the future of mRNA.

Dr. Caudle:
Wow. That is amazing. This is a great way to cap off our program. So, I'd like to thank you, Dr. Drew Weissman for sharing your insights on this continuing story on mRNA vaccines from how we got to here to where we're headed next. Dr. Weissman, it's great speaking with you, today.

Dr. Weissman:
Thank you very much.

Dr. Caudle
For ReachMD, I'm your host Dr. Jennifer Caudle and to access this episode and others from *VacciNation*, please visit ReachMD.com/VacciNation, where you can be part of the knowledge. Thanks for listening.

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