Expanding Role of mRNA Platform with Nobel Laureate Dr. Drew Weissman

We are excited to welcome Nobel Laureate Dr. Drew Weissman from the University of Pennsylvania yet again on CureTalks.

Dr.Weissman's groundbreaking research in messenger RNA (mRNA) technology earned him the Nobel Prize in Medicine, alongside his colleague Katalin Karikó. Their pioneering discovery in mRNA modifications enabled the rapid development and deployment of COVID-19 vaccines. These vaccines have significantly transformed global health outcomes.

In this episode, Dr. Weissman shares the latest advancements in mRNA platform and their expanding applications beyond infectious diseases. We will discuss how this transformative platform is paving the way for innovative treatments against diverse diseases, including celiac disease, cancer, HIV, autoimmune disorders, neurological and cardiovascular conditions.

Join us as we explore the exciting and expansive future of mRNA science with one of the world's foremost innovators.

Full Transcript:

Priya Menon: Hello and welcome to CureTalks. I'm your host Priya Menon. Today, we are delighted and honoured to host Noble Laureate, Dr. Drew Weissman from the University of Pennsylvania once again, on this platform. Dr. Weissman's groundbreaking research in mRNA Technology for which he shared the Nobel Prize with his Katalin Karikó has revolutionised vaccine signs and open doors to extraordinary medical possibilities. In this conversation today, we'll go beyond vaccines and explore the exciting potential of mRNA technology in treating diseases such as cancer, neurological conditions and more.

Joining us on the panel is. Jessica is an infectious disease epidemiologist and passionate science communicator known widely for her engaging work in public health education. Jessica will bring her unique perspective to this discussion. Jumping right in Dr. Weissman your pioneering work laid the foundation for transformative Covid vaccines, could you share with our audience a bit about your journey and what inspired your groundbreaking research in mRNA technology.

Dr. Drew Weissman: So, you have to look back about 30 years and the story is about Katie and I meeting at the Xerox machine are true. You'll have to explain to your young folks what a Xerox machine is, but we met, we started talking, we had completely different backgrounds, but as such turned out those backgrounds when combined led to the development of mRNA. I think what people have to realise is that we spent about 20 plus years with no funding, no publications, nobody cared about the work we were doing. And the reason why we didn't give up was that we would sit down and think about everything that could be done with mRNA, if we could solve the problems. And that's what kept us going. Now, we're at a stage where we can start doing all of those different things with mRNA, which is making the lab and the potential really enormous.

Priya Menon: Thank you, Dr. Weissman. I'm actually quite familiar with your story, your and Katalin's story. We discussed this last time as well but it is truly inspiring to think that for 20 years you relentlessly worked on something and kind of saved the world I should say. And I've also had the opportunity, Dr. Weissman, to talk to some of your lab colleagues, just after you won the Nobel and they would tell me that he's so down to earth. Even now he just walked into work like every other day. So that's truly, truly such a humbling experience, to be able to talk to you and to hear the story.

Today what we want to discuss is a little bit about the complexities that researchers face, when using this technology to say, tackle other challenging diseases, say like cancer or auto immune conditions. Can you talk a little bit about that?

Dr. Drew Weissman: Yeah. So, the original vaccine that was developed for covid19 and is also being used for many other infectious diseases, Influenza, HSV, HIV, norovirus, C. diff, malaria, TB, that the list keeps going on and on. That relies on an immune silent RNA with an adjuvanted LNP and the LNP stimulates the immune system in a way that it gives very potent antibodies and decent T-cell responses. So that's ideal for infectious diseases. We've now changed the LNP and changed the RNA somewhat, so NAP can make vaccines that have no adjuvanted activity. And what those vaccines do is they induce regulatory T cell that turn off immune responses and antigen specific manners. So we're using that to develop vaccines for allergies for peanut allergies, for dust mite allergies for other error allergens and food allergens. We're developing vaccines for autoimmune diseases. So, instead of giving an immune suppressive, an anti-TNF antibody methotrexate, cyclosporin etc that turn off the entire immune system, we selectively turn off only the auto antigen response. So, we believe it will be much safer and more effective. But, beyond that we're also working on cancer vaccines that we've all took to give better T Cell responses. We're developing Gene therapies for a variety of genetic disorders. Some of these are already in phase one clinical trials showing very good results. We've got programs for HIV cures, we've got programs to deliver therapeutic proteins to the brain, to the lungs, to the heart, to a variety of organs. So, we haven't thought of everything you can do with mRNA.

Priya Menon: So just for the audience, Dr. Weissman you mentioned LNP, which I believe is Lipid Nanoparticles, that help in delivering mRNA to T cells, is that right?

Dr. Drew Weissman: So, we have a big program delivery to T cells. That's currently in humans and phase one clinical trials. The first drug that we're going to develop with this is making car T cells transiently. So, what that can be used for? 6:53– For about I guess 4 years now, people have used CAR T cells that deplete B cells to treat autoimmune diseases. This includes things like systemic lupus, polymyositis, systemic sclerosis and a few others. You have to realise these are patients who come in, they fail drug therapy and they're dying, their kidneys are shutting down, they have encephalomyelitis, they don't have long to live, and what they do is they make CAR T cells the same way they do for B cell leukemias. And they've shown that about 90 percent of people become drug free and the other 10 percent they use a different kind of CAR and get them drug free. And some of these patients have been drug free for years. If you've ever taken care of a lupus patient, you never get them drug free. So, this is a phenomenal change. And what's happening is that we are resetting their B cell immune system which then helps reset the T cell immune system and it gets rid of the autoimmune characters in their disease. We're now doing that *in viva* which means people come in, they get a shot of RNA and they're done.

Priya Menon: That's remarkable. Dr. Weissman, I recently read a paper, an article from PENN, which talked about how mRNA technology was used to treat or even prevent celiac disease. Could you talk a little bit about the success?

Dr. Drew Weissman: Yeah, so that's a new program that Jilian Melamed in my lab is running, but that uses the same idea of turning off immune responses. So, for peanut allergies, it's an IGE immune response that's being targeted. For coeliac it's a different kind of immune response that attacks the GI tract and it's triggered by the coeliac protein. And we've identified and others have identified, a number of auto antigens that are involved in the immune response. So, what Jilian is doing is she's making immunosuppressive

vaccines that target those antigens. We have a great mouse model that was developed from the University of Chicago that's in use right now. We hope to be able to move to humans in the near future.

Priya Menon: Thank you, Dr. Weissman. I'll welcome Jessica into the conversation here to further enrich it. Jessica, please go ahead with your questions for Dr. Weissman.

Jessica Malaty Rivera: Hi Dr. Weissman. It's a pleasure to meet you. I, as Priya mentioned earlier, am an infectious disease epidemiologist, but I'm also a science communicator, which I spend a lot of my time making science makes sense for mostly lay audiences. And I think this is quite obvious, but we're talking about again that the Covid 19 pandemic created a lot of interest, but also, a lot of confusion about mRNA technology, mRNA vaccines in particular and so I'd love to know if you can help us understand some of the biggest misunderstandings that you even in your lab are trying to address.

Dr. Drew Weissman: So, if you look at vaccine hesitancy Edward Jenner was credited with the first vaccine where he took cow parks fluid and immunised people initially in England and protected them from smallpox. There are paintings and pictures right after that showing people getting vaccinated and growing cow heads out of their ears or out of their arms or off of their heads, people turning into cows. So, vaccine hesitancy isn't a new thing. In the old days, we usually thought of it as California hippies, who weren't interested in any kind of vaccines or medical therapies. What's different now is a combination that it's become a political issue and many hard-wright republicans consider if you take the vaccine, you're not really a republican.

And part of this seems to come out of a feeling for you can't make me do anything. None of this applies to medical science, the issue is more there is A social media infrastructure that is driven to attack vaccines, attack RNA. If you look the NPR did a story on this a couple years ago, they found 12 people who were responsible for 65 percent of the misinformation. And if you look at who they are, they are a combination of lawyers who sue pharmaceutical companies over supposed vaccine adverse events and physicians who sell made up homoeopathic, I don't know what they are, medications is not a good word and their spiel is that don't get the vaccine, take my therapy.

So, all of the misinformation is starting from people trying to rip off the public, trying to make money, but it's become a law. It's become part of our political system. Mark Twain had a quote from over a hundred years ago that said – "A lie makes it halfway around the world. By the time, the truth is putting the shoes on." – So it's just an enormous competition and the conspiracy theories get around the world and get into people's brains much more than the truth does. So, we're working on trying to develop better messages so people understand. But the misinformation about RNA includes The Surgeon General in Florida saying DNA gives you cancer. What he doesn't realise is that every vaccine made from a live virus, a killed virus, a subunit protein has DNA in it. The FDA limits the amount is the same for all of those vaccines, that's nonsense. There are crazy people who say the vaccine makes them magnetic. There are people who say Bill Gates puts chips in the vaccine. The misinformation is just wild, but people hear it and they trust the misinformation as much as they trust their personal doctors.

Jessica Malaty Rivera: Yeah, you are kind of speaking my language. I am quite familiar what the disinformation does and you mentioned, I work a lot on the intersection of epidemics and infodemics. And so, understanding, dynamics of information, and harmful information are not new concepts. I often talk about the smallpox, cowpox story as my origin story to for vaccine misinformation and conspiracies. Because again, it is not a new phenomenon by any means, but it's hopefully one that we can change. I've seen change, I have entered the deep end of social media and do most of my communication there. And I've seen some progress, but I've also seen some of the darkest disinformation of my life on social media. To bring it back to something positive, though the history of mRNA often comes up just the long runway to the Covid 19 vaccine that was often forgotten because people hear words like operation warp speed or even just seeing how quickly it was expedited which we know as scientists was just the removal of red tape and a well-oiled funded machine. I mean, you talked about not having funding yourself and you know how that puts everything to a screeching halt. Can you talk to folks about just the specific history roadmap of how we got to the mRNA vaccines for Covid? I know it, but I feel like a lot of people don't remember it.

Dr. Drew Weissman: Yes. So, when the vaccine was first released, I spent a lot of time, talking to lay audiences, most the evenings and weekends. I would be in churches, in community halls, on Zoom, talking to lay people about what the coronavirus epidemic was, what the vaccine is, what RNA is, how it works and why it's safe and why you need to take it. RNA vaccines have been in people since the late 90s, this is not new technology. What's new and what operation, what speed it took a technology that was already in development that had already been in phase one clinical trials and rapidly made a covid 19 vaccine. I used the joke with journalists who asked about it, about why maybe it was too fast. And my response was if we had taken two or three years, we would have been yelled at for being too slow. So, there was no way to win this argument and being fast, saved lives and to me, to physicians, in general, that's the most important thing.

Jessica Malaty Rivera: Yeah. I think a lot of folks are experiencing kind of that revisionist history of things that happen in covid. And in my research, we've done some sentiment analysis on vaccine technology in general. And it's interesting there seems to be a phenomenon of people partitioning vaccines as some being old school and some being new school, old-school ones being the ones that they remember from their childhood that are acceptable, but the new school ones, mRNA vaccines included, especially as they have heard in headlines that mRNA technology, might be considered for future flu vaccines or future paediatric vaccines. Those are considered new and so I'd love to know like how much of the mRNA technology do you think will be part of newer school vaccines and future vaccines?

Dr. Drew Weissman: So, I think that's going to depend on what country you're in. My fear is that in the United States the threat is they're going to cancel all RNA vaccines. A number of states are trying to pass laws, making it illegal to give RNA vaccines to all mammals. So not for food crops or for humans. That's hopefully going to be a short-term thing. People have to realise the covid 19 vaccine was the most tested vaccine ever. No vaccine has been tested more into the covid 19. And it's also considered one of the safest vaccines ever developed. So, those two things put together and its efficacy, its ability to cure people, to prevent disease make it a great vaccine approach. It's also really inexpensive to make. I have a big program setting up RNA infrastructures in low- and middle-income countries across the world. We've already built 15 GMP sites. And we're now building the infrastructure for those countries to develop their own RNA vaccines and therapeutics. The ideas that if they have access to the technology, they can develop vaccines for diseases that affect their population. So, we have collaborators in South America, making zika vaccines, and in Southeast Asia making Dengue, Tularemia, dust mites and others and Sub-Saharan Africa making malaria and TB. These are vaccines that big pharma has less interest in because the diseases in current parts of the world that don't have a lot of money and can't afford the development. If local researchers, local people can develop these vaccines for diseases that affect their populations, I think that's like a great way forward.

Jessica Malaty Rivera: Yeah, I mean I agree. Do you think that people should expect, if policies are not the hindrance, should people expect to see more mRNA vaccines in the future because of the fact that they're quite safe and very effective and also quick to reproduce and to make in bulk?

Dr. Drew Weissman: Certainly. So, there are over 300 clinical trials going on right now with new types of vaccines. What we have found is that we mostly concentrate on diseases where other vaccines have failed. And we have RNA working in those things, things like norovirus, which is the cruise ship disease and __ which is a serious disease used to be for hospitalised patients, now it is community acquired. Many vaccines have tried in these diseases and failed. We have RNA vaccines that look like they're going to work.

Jessica Malaty Rivera: Alright. I can't wait for a vaccine from norovirus. I'm a mum to three young kids and I hope to never see that disease again. mRNA vaccine refusal has not disappeared and I'm curious, what are some ways beyond repeating the fact that it's safe and effective and it's the most scrutinised studied vaccine, particularly the covid 19 one. What are some approaches that we can use to build greater public confidence in this, in specific innovation type?

Dr. Drew Weissman: Yeah, unfortunately in the old days people used to rely on their leaders. So that was there, from their religion, from their community, from the government, to lead them to tell them, this is safe,

you should do it and that has broken down. I have people dying of measles. My big fear is they're going to start dying from other easily preventable diseases. And my biggest fear, we've had polio cases in the U.S before, if polio comes back that's an incredibly dangerous situation and the rates of vaccination keep dropping. So, to me, it's a community, government, country-wide issue to improve vaccination. And my biggest fear is that the only thing that's going to drive it is when lots of kids start dying.

Jessica Malaty Rivera: If it's any consolation in the work that I do on trust and measuring trust has shown that while trusted institutions is shaky right now. People trust people because of the power of storytelling and so the community organising and community messengers and trusted messenger programs are growing, and are continuing to try to get those messages deeper to harder to reach communities to communities, who have been targeted and prayed upon. I'm trying to stay as optimistic as I can because these are unprecedented times and I'd love to end on a high note in that sense. Could you share what is the most exciting and closest breakthrough in this technology that gets you hopeful?

Dr. Drew Weissman: So, what we have what we think is a fantastic new therapy. It's a gene therapy that will first be applied to sickle cell anaemia. There have been two gene therapies approved for sickle cell last December. But what they do is they take a lot of bone marrow out of a patient. They culture it in the lab, they add a lentivirus that delivers an enzyme that changes the genome. They then give the patient high dose chemotherapy and transplant the bone marrow back in. It works. Patients are being cured of sickle cell with this. It's predicted to cost. 3.2 million dollars a patient, 300 000 people a year are born with sickle cell mainly in sub-Saharan Africa but throughout the world, 3.2 million dollars and fancy hospitals with the laboratory infrastructure to do this Gene therapy don't exist in Africa, in Asia, in Latin America. What we've developed is we can now target bone marrow stem cells in Vivo And we can deliver gene editing enzymes. So, the RNA doesn't do anything to the DNA but the enzyme that's encoded, it's from the Cas 9 family that specifically fixes genetic mutations and should cure sickle cell anaemia. So, my dream one day bring in an igloo cooler full of RNA to sub-Saharan Africa and have people line up and get shots of RNA LNPs and cure their sickle cell anaemia. I don't know what the final cost would be, but it's not going to be millions of dollars. That can then be applied to the thousands of other genetic disorders of the bone marrow.

Jessica Malaty Rivera: That's beautiful. And that's a world that I want to live in and I hope that that is achieved. Dr. Weissman, I'm so thankful for the work that you do. I wish you continue in success and continue in endurance. Because again, this is unprecedented times right now. Priya, thank you for the opportunity to do this as well.

Priya Menon: Thank you, Jessica, thank you for sharing that. Dr. Weissman I was going to ask you about the exciting thing, most exciting thing for you, but Jessica already asked you that. So, I'm going to ask you a different question, can you share some unique huddles that your team faces when doing research on mRNA, in technology as compared to probably anything else, something different, something unique other than funding and what's happening or something in the lab that only you are aware of.

Dr. Drew Weissman: Yeah. The hurdles are being the same as all other research. It's relying on animal models, its being able to get money to do the research we want. I now spend a lot of my time and I talked about this earlier, developing RNA infrastructure across the world to give better equity for RNA and we're hopefully will get more funding for that soon. But to me that's the biggest hurdle right now, is building RNA research clinical trials regulatory experience, GMP production and drug distribution throughout the world. The other way that that's going to be important is we're going to have another pandemic. I don't know if it's going to be a coronavirus or an influenza, or something else unexpected, but, it's guaranteed. We have pandemics every certain number of years 20-30 in that neighborhood, so there will be more. If we have 15 sites in low-end middle-income countries that can rapidly respond and make a vaccine, that will give us drug distribution across the world. For the covid 19, the U.S, Western Europe and a few other countries had vaccines in December of 21. It took Africa, Latin America, Southeast Asia over a year before they got any RNA vaccines. And to me that's a big problem, so we're trying to address that.

Priya Menon: Thank you. Thank you very much Dr. Weissman and Jessica for this insightful and engaging

conversation about the future of mRNA therapeutics. Thank you also to the University of Pennsylvania, and to our audience for joining us today. Stay curious, informed and we'll see you next time on CureTalks. Thank you everyone.