Transcript Details
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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Exploring Emerging Vaccine Technologies: Where Are We Headed?

Announcer:
Welcome to *VacciNation* on ReachMD, sponsored by Moderna. On this episode, we'll hear from Dr. Jeniffer Hernandez, Associate Professor of Biopharmaceutical Sciences at the Keck Graduate Institute, about where we're headed with vaccine technology. Here's Dr. Hernandez now.

Dr. Hernandez:
DNA vaccines and mRNA vaccines have been under development for the last three decades, since the 1990's. Recombinant vector vaccines– not that much research has been on those. DNA vaccines and mRNA are very similar in that they will most likely be the future of vaccinology. What is a DNA vaccine? A lot of you are probably familiar with mRNA vaccines, where the mRNA is injected, it goes into the cell or is taken up by innate cells of the immune system, and it's directly made into protein in the cytoplasm. DNA vaccines are different in that its DNA is small circular plasmid of DNA that has to go from the cytoplasm of the cell into the nucleus, so that's a little bit more challenging. Once in the nucleus, it gets made into mRNA, and then the mRNA goes into the cytoplasm and gets made into protein, so it's extra steps. mRNA vaccines came out way faster. They were approved because they are able to produce a strong immune response compared to DNA vaccines. DNA vaccines are still being kind of worked on. They kind of have to improve the protein expression from the DNA vaccine, once it's made mRNA. Some groups are maybe thinking about adding adjuvant to boost the immune response. There is one example of a DNA vaccine forCOVID-19, or the SARS-CoV-2 virus. It's called, ZyCoV-D, which was developed in India, and that's actually being used in India, and they've had good efficacy, not as great as the mRNA vaccines. It's around 67% effective, but that's effective against the Delta virus, so that's still pretty good. But like I said, it's not as robust as the mRNA vaccine but that could be a good thing. The mRNA vaccine, as you know, can produce a strong immune response. Some people develop strong reactions towards it. That may not happen with DNA vaccines, because they provide not as a strong immune response, so, it's not as immunostimulatory as an mRNA vaccine. They're very similar. Both are very inexpensive to make. DNA vaccines are actually more stable than mRNA vaccines, because DNA is double-stranded, so it can be at room temperature for three months, because DNA is double-stranded. You can find DNA from dinosaur bones, right? It can last longer in refrigerated temperatures, like four to eight degrees, whereas immuno-mRNA vaccines have to be stored in the freezer, from -20 to -80, and they last about six months. So that's an advantage, because you can go to rural areas or areas that are under poverty, and you don't have to deal with refrigeration or freezer to transport the vaccines like you have to worry about with mRNA vaccines.

DNA vaccines are kind of right up there with mRNA vaccines. It's just mRNA vaccines have been faster to come on the market because they're more robust and they provide a stronger immune response. The DNA vaccine that was produced in India, you actually need three shots to have that 67 protectivity against the COVID-19 Delta variant, and the Pfizer and the Moderna vaccine – the mRNA vaccine –you only need two shots. That's one of the challenges with the DNA vaccines. They're not as robust. You need three doses. The difficulty there is getting the DNA vaccine into a nucleus, because the mRNA vaccine has to go into the cytoplasm and it's made into protein. So that makes a little bit more robust. You inject the DNA vaccine, maybe not all of it gets into the nucleus, and so that decreases the amount of protein that's going to be made, right? Not all of it can get into the nucleus. Those are some of the challenges with DNA vaccines, but they're already being used for protection against COVID-19. And there's several other DNA vaccines that are being studied, and that are undergoing in human trials. Not just for COVID-19, but also HIV, Ebola, Zika, HPV, herpes there's a lot of human trials for targeting different infections with the DNA vaccine. Hopefully, not just mRNA vaccines will be the future of vaccinology, but also DNA vaccines.

The other one was recombinant vector vaccines. Those use adenovirus from chimpanzees. Those don't cause any symptoms in patients, but those have been genetically engineered to express the spike protein, for example. The spike protein that's used to attach

to the surface of cells and get into the cells and infect the cells. One example is actually the Johnson and Johnson vaccine. They use this adenovirus that cannot replicate, so they take out the machinery for the virus to make more virus, and they put in the genes for a spike protein. That's what a recombinant vector vaccine is. There's also recombinant proteins, that you basically take the spike protein and inject that into patients. The recombinant proteins and the recombinant vector vaccines – they're much more difficult to design and they take a lot of time, because you have to engineer the adenovirus from the chimpanzee so it doesn't reproduce within the host It doesn't actually reproduce enough to cause some kind of symptoms. That's two examples of the new types of vaccines that are in the works or have already been tried in humans.

Announcer:
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