Why COVID-19 vaccine research remains critical

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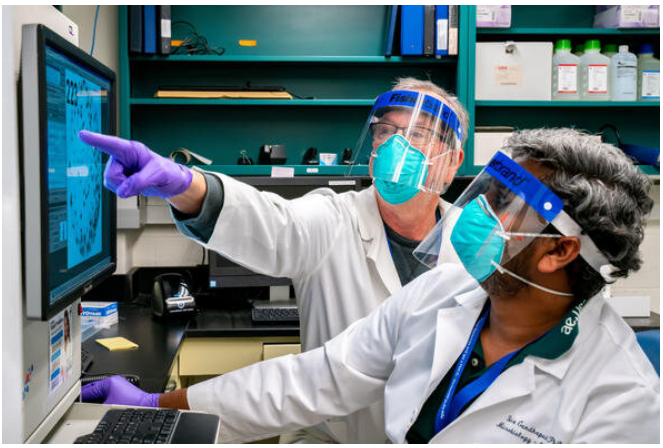

UK vaccine researcher Jerry Woodward weighs in on why research remains critical even as first COVID-19 vaccines released. Credit: Ben Corwin, Research Communications

While the Pfizer and Moderna COVID-19 vaccines continue to be administered across the United States under an emergency authorization status, ongoing coronavirus vaccine research and development remain critical to the fight against the global pandemic.

The emergency authorization allows us to protect people now, but research will continue for decades, says University of Kentucky College of Medicine vaccine researcher Jerry Woodward.

Woodward, a professor of Microbiology, Immunology and Molecular Genetics, is one of several UK medical researchers currently focusing on COVID-19 treatments, preventions and outcomes. Woodward is currently working on a preclinical study for a promising COVID-19 vaccine candidate, as well as directing a study testing antibodies and T cells to determine how long immunity lasts for patients who have had COVID-19.

Woodward weighed in with UKNow about why it's critical to continue COVID-19 vaccine development and research.

What do the recent authorization and administration of COVID-19 vaccines mean for other vaccines currently in development?

There are currently dozens of potential COVID vaccines in some stage of testing around the world and several of them are in the pipeline for approval and use in the future. For many of them, the success of the Pfizer and Moderna vaccines is very positive.

These two vaccines target SARS-CoV-2's spike protein, which is how the coronavirus attaches to and infects host cells. Because of work on the SARS virus (which has a similar spike protein to SARS CoV-2) over the last 15 years, scientists were able to focus on targeting the spike protein with some confidence. All of the vaccine trials to date confirm that targeting the spike protein is sufficient to make an effective COVID-19 vaccine. It brings a strong rationale to keep many vaccine development programs going.

What is the difference between the Pfizer and Moderna vaccines and the others being developed?

The Pfizer and Moderna vaccines are based on what is called a messenger RNA, or mRNA, which produces the SARS-CoV-2 spike protein by introducing RNA into cells near the site of injection. The RNA gives those cells the genetic code to produce the spike protein, which then triggers the immune system to fight the virus.

A couple of the other frontrunners, including the AstraZeneca and the Johnson & Johnson (Janssen) vaccines, are based on an adenovirus vector, which instead uses a harmless virus that cannot replicate but releases genes into cells to

encode the SARS-CoV-2 spike protein.

Instead of using mRNA or adenovirus vectors, other vaccines focus on injecting the spike protein directly. This is the type of vaccine that my lab has been working on and is historically a more "tried and true" platform. This category—called protein-based or subunit vaccines—represents the vaccines that have been mostly approved recently in other areas like influenza, human papillomavirus (HPV) and hepatitis B.

Why is it important to continue developing COVID-19 vaccines?

One of the reasons is scale up. It's very typical to have multiple types of vaccines to protect against the same disease. In the case of the global need for a COVID-19 vaccine, Pfizer and Moderna are probably not going to be able to supply enough for the demand. Companies have other vaccines that are based on different platforms and some of them are easier to make and distribute in different countries. Therefore, some of them are easier to scale up. A related issue is cost and logistics of distribution: for example, requiring a temperature-controlled supply chain, which is particularly important for countries without a good health care infrastructure.

Another issue is safety and efficacy in different demographics or age groups. Right now, we have no data yet on the safety and efficacy of the vaccine in children or pregnant women. It is possible that a particular vaccine platform will be better suited to one of these groups.

How will vaccines be evaluated?

While approved vaccines are able to prevent a COVID reinfection with a high effectiveness rate, it is still early on and we don't know how durable they are going to be in the long run. We also don't know how effective these vaccines are at preventing asymptomatic spread. These questions are what researchers in my field will be looking at for many years to come.

There are two parts that researchers look at when analyzing the immune response to a vaccine: the first is antibodies and the other is T cells, which are white blood cells that protect against a disease by killing infected cells and assist in the production of antibodies. T cells are particularly important because they last far longer than antibodies. For example, T cells specific to the SARS virus have been found in people 10 years after infection.

We don't yet know how good any of the COVID-19 vaccines are at creating a T cell response or how long the T cell responses are going to last. So there are many questions that still need to be answered. That is another reason why different vaccine platforms—like mRNA, adenovirus vector or subunit vaccines—need to be developed and studied in parallel. While all may be effective, we may find that some may create a longer immune response than others. We just don't know at this point.

What do recent COVID-19 mutations mean for vaccine research moving forward?

All viruses mutate as they spread in the population, and mutations that increase the fitness of the virus (for example, increase the ability to spread or avoid immune responses) will tend to be amplified. The good news is that it is hard for a virus to avoid the immune response by mutation because our antibodies and T cells recognize different parts of the virus. Influenza is very good at this, but SARS-CoV-2 has not yet mutated in a way to avoid our immune response. The recent mutated strains identified first in the United Kingdom and now in the U.S. appear to make the virus more transmissible, but they are still effectively dealt with by our current vaccines.

Influenza has taught us that a virus can mutate and escape our vaccine-induced immunity. Therefore, there needs to be a worldwide effort to completely sequence SARS-CoV-2 viruses and to identify early-on whether any of these mutations could reduce our vaccine-induced immunity to that strain. If such a strain is found with mutations in the spike protein, for example, then the new spike protein can be rapidly produced and added to our current vaccines, much as we do now for influenza vaccines.

Finally, new coronaviruses and other viruses will

continue to cross over from animals to the human population and we need to be ready to rapidly mobilize our vaccine production to deal with these new threats. We are lucky that enough researchers were working on the immune response to the original SARS virus long after the global outbreak was contained in 2003. This provided critical baseline information and allowed us to develop the SARS-CoV-2 vaccine in record time. The lesson is that vaccine and infectious disease research needs to continue at a high level, long after the pandemic is over. The time to repair your roof is when the sun is shining.

Provided by University of Kentucky