Dr. Delgado COVID-19 Update 07-31-20

More On Vaccines

The colossal impact of the coronavirus is motivating the speed, opening a spigot of funding and inspiring research teams around the world to join the hunt. But the astonishing pace of the progress is also a consequence of the virus itself: It is, scientifically speaking, an easier target for potential vaccines than other pathogens.

Just six months ago, when the death toll from the coronavirus stood at one and neither it nor the disease it caused even had a name, a team of Chinese scientists uploaded its genetic sequence to a public site. That kicked off the rush to develop a potential vaccine.

Vaccines typically take years, if not decades, to reach people; the record now is four years for the mumps vaccine.

The fact that the culprit was a coronavirus — one that was strikingly similar to others that had previously leapt from animals to people — meant scientists could quickly

reconfigure vaccine projects in the works for those. Many of the teams pursuing vaccines for Covid-19 (SARS-CoV-2) have previously worked on vaccines for the original SARS virus, which caused a 2003 outbreak and MERS, which has caused over 2,500 cases since it started spreading in 2012.

The earlier projects had pointed to a component of the coronaviruses called the spike protein as a ripe target for a vaccine, which gave scientists a head start for crafting their candidates. These previous efforts illuminated stumbling blocks that have been avoided presently in designing the coronavirus vaccine.

How does it work?

Vaccines train the immune system to recognize a pathogen it hasn't yet encountered. Normally, our immune system builds that memory by battling an infection, so that it can halt a virus in its tracks should it try to invade a second time. A vaccine acts like that first exposure, but without making people ill.

With Covid-19, researchers are working with new ways of providing that first look, building vaccines on adaptable

platforms engineered to possibly pivot from pathogen to pathogen.

Older strategies for developing vaccines, such as obtaining the virus and weakening or inactivating it, are lengthy processes. But the new cutting-edge approaches require scientists only to know the virus' genetic sequence. With that, they can string together the right pieces of code to synthesize vaccines.

That's allowed scientists to move with record speed. Less than 10 weeks after the Chinese scientists published the SARS-CoV-2 sequence, a team from the National Institute of Allergy (NIAID) and Infectious Diseases in conjunction with the biotech company Moderna had a candidate ready for a Phase 1 trial.

The Moderna/NIAID vaccine was built with **mRNA**, a piece of genetic code containing the instructions for the coronavirus' spike protein. The vaccine shuttles the mRNA into cells, which "read" those instructions and churn out the protein — providing the immune system with that first peek to the spike, like giving a hound a scent.

Another company called Inovio is pursing a similar vaccine

model using **DNA**, a different genetic material. Neither an mRNA nor a DNA vaccine has been approved before.

Other approaches, including Johnson & Johnson and a collaboration between Oxford University and AstraZeneca — are attaching the gene for the spike protein to another, harmless virus that ferries it into cells. There, it gets expressed into the spike, allowing the immune system to mount its forces. Another company, Novavax, is directly producing versions of the spike from the gene itself and using them directly in its vaccine. This is pretty novel stuff and the ingenuity being applied by scientists to meet this head on is truly scientifically revolutionary.

The focus on the spike protein is a strategic choice. The proteins, which give SARS-CoV-2 the crown-like appearance that's characteristic of coronaviruses, attach to receptors on people's cells, allowing the virus to enter and replicate. By blocking spike proteins, these vaccines could prevent infection.

Production/Approval

One reason vaccine development is so slow normally is because companies want to see candidates successfully

pass through each sequence in the development process before sinking funding into the next phase. Most vaccine candidates don’t proceed to completion and the inherent risks financially can be limiting.

The current government and foundation contracts in the billions aren’t just to cover the research and trials; it’s mostly to get companies to hedge their bets start manufacturing their products — even though their vaccines might not prove to be effective. It’s necessary to ensure that any authorized vaccine can be rolled out to as many people as quickly as possible.

Many lessons were learned during the Ebola crisis, when regulators embraced a new found dexterity in green-lighting vaccine trials and took a more proactive approach to communicating with companies about the efficacy thresholds products needed to meet. That’s continuing with Covid-19: the Food and Drug Administration, for example, has outlined that vaccines need to prevent infections or reduce the severity of Covid-19 in 50% of recipients to be approved.

Normal clinical trials include three increasingly larger phases that establish how safe and effective a drug or vaccine is. But with the Covid-19 pandemic, some of the

trials have been collapsed into Phase 1/2 or Phase 2/3 trials. This flexibility has allowed potential candidates to shave weeks or months off the process by saving research teams from having to write new protocols or get additional clearances as they move forward.

Will it work?

What's that saying? That speed can kill? Some groups have questioned how such a fast-moving process can ensure safety. They want assurances that the efficacy and safety standards will not be compromised to the detriment of our citizens in a quest for any vaccine candidate prior to appropriate due diligence. Public health experts say vaccine makers need to be transparent that while manufacturing and regulatory steps are being streamlined, safety checks aren't being sacrificed.

It's also not clear yet what a vaccine "working" will look like. A Covid-19 vaccine might be like the flu vaccine — only preventing infections in some people, or staving off serious disease, but still leaving people contagious.

A vaccine that prevents even 50% of infections would be a massive lifeline. But I worry there's a disconnect between a public expecting vaccines to instantly reset

their lives and what the first vaccines may actually allow.

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