The 'key' to new COVID-19 vaccine development

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New variants of the SARS-CoV-2 virus most likely will necessitate the development of more vaccine options in the years ahead, and a biomedical scientist at Iowa State University believes the 'key' to that development lies in the way the virus binds to human cells.

Michael Cho, a professor of biomedical sciences at Iowa State, is studying how to develop COVID-19 vaccines that target SARS-CoV-2's receptor-binding domain, or the part of the virus that docks with the host cellular receptor, angiotensin converting enzyme 2 (ACE2). This docking process allows the virus access to the host's cells, which leads to infection.

Cho was the lead author of a study recently published in the peer-reviewed scientific journal *Frontiers in Immunology* detailing the ability of a vaccine to induce antibodies in mice that target the virus's receptor binding domain. The patent-pending vaccine approach is available for licensing from the Iowa State University Research Foundation. Cho will deliver a virtual presentation on the potential of the approach to BioConnect Iowa's vaccine and immunotherapeutics meeting on Wednesday.

The antibodies produced by the experimental vaccine attack the receptor binding domain, or RBD, of the virus. The RBD is the portion of the viral spike protein that binds to host cells to initiate infection. Cho likens the spike protein to a key, and the RBD is the part of the key that actually enters the lock.

"The spike glycoprotein is the key that opens the lock, and the region of the key with all the peaks and valleys and grooves is the RBD," Cho said. "If antibodies attack the RBD, then the key won't work and the door will stay locked, preventing infection. We don't really need to make antibodies against the entire spike protein, which is more difficult to make. We can just focus on the RBD portion."

This approach differs from the three vaccines currently available in the United States to ward off COVID-19. The mRNA vaccines produced by Pfizer and Moderna work by delivering a set of instructions that teach the immune system how to make the entire spike protein that triggers an immune response. The Johnson & Johnson vaccine is known as a viral vector vaccine that uses a modified version of a different virus.

Cho and his colleagues conducted trials of the RBD subunit protein vaccine on mice and were able to induce a potent antibody response in the rodents over the course of three injections. The study showed that one or two injections are sufficient, depending on the adjuvant used. Cho said he would like to test the approach in human trials.

Easy to produce, scale up

The RBD-targeting vaccine has some advantages over the vaccines currently licensed for use in the United States. Cho said the experimental vaccine is relatively easy to produce and scale up because it

requires only a small portion of the virus's spike protein to manufacture. The RBD vaccine also can be delivered multiple times, which could be necessary to develop immunity against multiple virus variants that will inevitably emerge.

Cho said the process of reaching herd immunity to COVID-19 through vaccines will take time, allowing for new variants of the virus to spread. This is particularly true for populations in developing countries that have had only limited access to the currently available vaccines so far. And as more variants emerge, the likelihood grows that additional vaccines will become necessary, he said.

"Just because we have vaccines now, that doesn't mean we won't need more in three or five years, maybe even longer," he said. "I don't think our vaccine is too late to play a role."

The 2021 Immunotherapeutics Virtual Conference is presented by Iowa State, the University of Iowa and BioConnect Iowa. The conference aims to connect cutting-edge university research with industry leaders. Cho will address the virtual conference Wednesday morning. Registration information is available at www.isupark.org/news/registrat … apeutics-conference/.

More information: Ling Niu et al, A Structural Landscape of Neutralizing Antibodies Against SARS-CoV-2 Receptor Binding Domain, *Frontiers in Immunology* (2021). DOI: 10.3389/fimmu.2021.647934

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