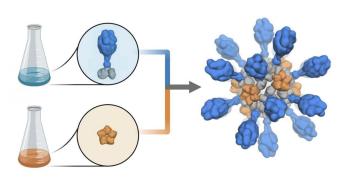


Ultrapotent COVID-19 vaccine candidate designed via computer

2 November 2020



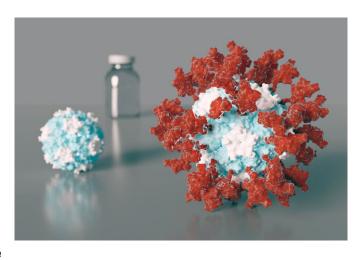
Production schematic shows how coronavirus proteins are added to a computer-designed nanoparticle platform to create a candidate vaccine against COVID-19. The vaccine candidate was designed and tested in animal models by researchers at the University of Washington School of Medicine Credit: Ian Haydon/UW Medicine Institute for Protein Design

An innovative nanoparticle vaccine candidate for the pandemic coronavirus produces virus-neutralizing antibodies in mice at levels ten-times greater than is seen in people who have recovered from COVID-19 infections. Designed by scientists at the University of Washington School of Medicine in Seattle, the vaccine candidate has been transferred to two companies for clinical development.

Compared to vaccination with the soluble SARS-CoV-2 Spike protein, which is what many leading COVID-19 vaccine candidates are based on, the new nanoparticle vaccine produced ten times more neutralizing antibodies in mice, even at a six-fold lower vaccine dose. The data also show a strong B-cell response after immunization, which can be critical for immune memory and a durable vaccine effect. When administered to a single nonhuman primate, the nanoparticle vaccine produced neutralizing antibodies targeting multiple different sites on the Spike protein. Researchers say this

may ensure protection against mutated strains of the virus, should they arise. The Spike protein is part of the coronavirus infectivity machinery.

The findings are published in *Cell*. The lead authors of this paper are Alexandra Walls, a research scientist in the laboratory of David Veesler, who is an associate professor of biochemistry at the UW School of Medicine; and Brooke Fiala, a research scientist in the laboratory of Neil King, who is an assistant professor of biochemistry at the UW School of Medicine.



Artist's depiction of an ultrapotent COVID-19 vaccine candidate in which 60 pieces of a coronavirus protein (red) decorate nanoparticles (blue and white). The vaccine candidate was designed using methods developed at the UW Medicine Institute for Protein Design. The molecular structure of the vaccine roughly mimics that of a virus, which may account for its enhanced ability to provoke an immune response. Credit: Ian Haydon/ UW Medicine Institute for Protein Design

The vaccine candidate was developed using structure-based vaccine design techniques invented at UW Medicine. It is a self-assembling protein nanoparticle that displays 60 copies of the



SARS-CoV-2 Spike protein's receptor-binding domain in a highly immunogenic array. The molecular structure of the vaccine roughly mimics that of a virus, which may account for its enhanced ability to provoke an immune response.

"We hope that our nanoparticle platform may help fight this pandemic that is causing so much damage to our world," said King, inventor of the computational vaccine design technology at the Institute for Protein Design at UW Medicine. "The potency, stability, and manufacturability of this vaccine candidate differentiate it from many others under investigation."

Hundreds of candidate vaccines for COVID-19 are in development around the world. Many require large doses, complex manufacturing, and cold-chain shipping and storage. An ultrapotent vaccine that is safe, effective at low doses, simple to produce and stable outside of a freezer could enable vaccination against COVID-19 on a global scale.

"I am delighted that our studies of antibody responses to coronaviruses led to the design of this promising vaccine candidate," said Veesler, who spearheaded the concept of a multivalent receptor-binding domain-based vaccine.

More information: Alexandra C. Walls et al, Elicitation of potent neutralizing antibody responses by designed protein nanoparticle vaccines for SARS-CoV-2, *Cell* (2020). DOI: 10.1016/j.cell.2020.10.043

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