



This document is scheduled to be published in the Federal Register on 10/01/2020 and available online at [federalregister.gov/d/2020-21708](https://www.federalregister.gov/d/2020-21708), and on [govinfo.gov](https://www.govinfo.gov)

[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The invention listed below is owned by an agency of the U.S. Government and is available for licensing to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION CONTACT: Amy F. Petrik, Ph.D., 240-627-3721; amy.petrik@nih.gov. Licensing information and copies of the U.S. patent application listed below may be obtained by communicating with the indicated licensing contact at the Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, 5601 Fishers Lane, Rockville, MD, 20852; tel. 301-496-2644. A signed Confidential Disclosure Agreement will be required to receive copies of unpublished patent applications.

SUPPLEMENTARY INFORMATION: Technology description follows:

Structure-Based Design of SARS2-CoV-2 Spike Immunogens Stabilized in the RBD-All Down Conformation.

Description of Technology:

SARS-CoV-2 has emerged as a global pathogen, sparking urgent vaccine development efforts. The trimeric SARS-CoV-2 spike appears to be a leading vaccine antigen. However, the inability of antibodies such as CR3022, which binds tightly to a cryptic spike epitope, to neutralize SARS-CoV-2 suggests a spike-based means of neutralization escape.

Researchers at the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID) sought to understand how antibodies with high affinity fail to neutralize the SARS-CoV-2. To that end, the researchers characterized the SARS-CoV-2 spike protein conformational changes as a function of pH and observed that at endosomal pH the spike protein has a conformation in which all of the receptor binding domains (RBD) are in a down conformation which could explain the virus' ability to escape neutralization in the endosome.

Hypothesizing that SARS-CoV-2 escapes neutralization through pH-dependent conformational masking, the researchers designed spike proteins with mutations to stabilize the spike in the RBD-all down conformation. Such designs include cavity-filling mutations, disulfides, aspartic acid to asparagine mutations, proline mutations, and other sequence modifications to fix the spike protein in its RBD-all down

conformation so that immunization at a physiological pH will elicit antibodies that can recognize the low pH-stabilized all RBD-down conformation of the spike protein and no longer be susceptible to pH-induced neutralization escape.

Immunogenicity studies are underway to determine which of the designs will yield a neutralizing immune response in mice. Pending results in mice, a lead candidate will be selected for studies in nonhuman primates.

This technology is available for licensing for commercial development in accordance with 35 U.S.C. § 209 and 37 CFR Part 404.

Potential Commercial Applications:

- An improved stabilized spike immunogen for the development of protective SARS-CoV-2 vaccine.

Competitive Advantages:

- Stabilized SARS-CoV-2 spike variants with potential to elicit higher levels of neutralizing antibodies than current related vaccine development.
- Identification of a methodology to screen for improved spike variants (by assessing binding by neutralizing versus non-neutralizing antibodies).

Development Stage: Preclinical Research.

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Publications: Zhou, T *et al.*, (2020). Cryo-EM Structures Delineate a pH-Dependent Switch that Mediates Endosomal Positioning of SARS-CoV-2 Spike Receptor-Binding Domains. *BioRxiv*.

Intellectual Property: HHS Reference Number E-187-2020 includes U.S. Provisional Patent Application Number 63/046,603, filed 06/30/2020.

Licensing Contact: To license this technology, please contact Amy F. Petrik, Ph.D., 240-627-3721; amy.petrik@nih.gov.

Dated: September 17, 2020.

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[FR Doc. 2020-21708 Filed: 9/30/2020 8:45 am; Publication Date: 10/1/2020]