STABILIZING AN ALTERNATIVE CONFORMATION OF THE SARS-COV-2 SPIKE PROTEIN

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PATENT STATUS

Country	Type	Number	Dated	Case
Patent Cooperation Treaty	Reference for National Filings	2023/283447A3	06/01/2023	2021-173

Patent Pending

BRIEF DESCRIPTION

Researchers at UC Berkeley have developed methods to probe the conformational landscape of the SARS-CoV-2 Spike protein in the prefusion and ligand binding variations.

The Spike protein from SARS-CoV-2 is the primary target for current vaccines against COVID-19 and is the focus of many therapeutic efforts. This large, heavily glycosylated trimeric protein is responsible for mediating cell entry via recognition of host cell receptors. A stabilized prefusion version of the structure of the Spike protein (termed S-2P) has been widely used for vaccine development and many structure/function studies, which have demonstrated that like other class 1 viral fusion proteins, the SARS-CoV-2 Spike protein is dynamic and samples several different conformations during its functional lifecycle. However, there are few experimental studies on the dynamics within the pre-fusion state of the SARS-CoV-2 Spike protein. The protein's conformational landscape and the effects of perturbations, such as ligand binding (including receptor and antibody binding) or amino acid substitutions in emerging variants of concerns, are unknown.

Stage of Research

The inventors have developed hydrogen-deuterium exchange monitored by mass spectrometry (HDX-MS) methods to probe the conformational landscape of the soluble spike prefusion ectodomain, as well as the effects of ligand binding and sequence variation. They uncovered a stable alternative conformation that interconverts slowly with the canonical prefusion structure. This conformation is an open trimer, with easily accessible RBDs that expose the S2 trimer interface, providing new epitopes in a highly conserved region of the protein.

SUGGESTED USES

- Continuous-labeling HDX-MS on Spike-2P
- Identification of alternative S protein conformations and interconversion between conformations
- Examining effects of sequence changes on S protein structure and conformation
- Examining the effects of ligand binding on S protein structure and conformation

ADVANTAGES

- Dynamic structural modeling for S protein conformational changes based on sequence substitutions or ligand binding
- Examining new functional roles for structural intermediates and identifying potential new druggable sites

RELATED MATERIALS

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OTHER INFORMATION

KEYWORDS

Spike protein, Structure, Conformation, Mass spectrometry, Modeling

CATEGORIZED AS

- **Biotechnology**
  - Health
- **Medical**
  - Vaccines

RELATED CASES

2021-173-0

» Costello, S.M., Shoemaker, S.R., Hobbs, H.T. et al. The SARS-CoV-2 spike reversibly samples an open-trimer conformation exposing novel epitopes. Nat Struct Mol Biol 29, 229–238 (2022). https://doi.org/10.1038/s41594-022-00735-5

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

▶ Nanopore Sequencing of RNA Using Reverse Transcription

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