Docket #: S23-308

Compositions and Methods Related to Coronavirus Therapies

Researchers at Stanford have developed fusion proteins, containing ACE2 domain linked to a fragment of non-neutralizing anti-SARS-CoV-2 spike protein antibody, with a greater breadth of protection than previously described similar fusion proteins.

Coronaviruses are a large family of viruses that cause illness ranging from the common cold to more severe diseases, including Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). Coronaviruses are zoonotic, meaning they can be transmitted between humans and animals. Viral mutation and zoonotic transfer are anticipated to lead to future pandemics and largescale outbreaks. Indeed, the COVID-19 respiratory disease likely originated in bats, and led to a pandemic with over 750 million cases and nearly seven million deaths worldwide. To date, there are a limited number of active pharmaceutical agents that are effective at treating COVID-19 or other coronavirus infections in patients. There is therefore an urgent need for therapeutics capable of treating infections arising from known coronaviruses, as well as from new coronaviruses that will arise in the future. For instance, the development of monoclonal antibody (mAb) therapies was a major advance in the treatment of COVID-19. However, known mAb therapies gradually become ineffective with the emergence of new SARS-CoV-2 variants.

Stage of Development
Research – in vitro

Stage of Research
The inventors have developed improved fusion proteins containing an antibody domain, that binds a highly conserved epitope of betacoronavirus Spike proteins on the S2 subunit, and an ACE2 domain, which serves at the neutralizing domain. SARS-CoV-2 variants are less likely to escape the binding of fusion proteins than neutralizing mAbs targeting the RBD of SARS-CoV-2 Spike proteins.

Applications

- Use as a broad and high-potency therapeutic against coronavirus infections.
- Fusion protein therapies, which are likely to inhibit any betacoronavirus that uses the highly conserved ACE2 as a receptor, making them suitable for stockpiling in anticipation of the next betacoronavirus jumping from animals to humans.
- Use in high-risk patients with complex medication regimes.

Advantages

- Greater breadth of protection than previously described fusion proteins.
- The use of fusion proteins with enzymatically inactive ACE2 (the virus' own host receptor), which prevents adverse side effects of administering fusion proteins with active ACE2 domain. These adverse effects stem from the functions of ACE2 in regulating blood pressure and vascular tone.
- More efficacious in vitro activity than known anti-coronavirus mAbs.
- Broad neutralizing range that includes all tested SARS-CoV-2 variants and SARS-CoV-1.
- Expected to have few, if any, interactions with other medications a patient may be taking.

Innovators

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