Docket #: S20-215

Method of Treating Coronavirus Infection

Technology Reference
Stanford ref. no. S20-215
CZ Biohub ref. no. CZB-171S

Researchers at Stanford University have developed a novel treatment for coronavirus infection.

Coronavirus infections are endemic in humans and were the causative pathogen in up to 30% of seasonal upper respiratory infections prior to 2020. Several coronaviruses of interest including MERS, SARS-CoV1, and SARS-CoV2 have emerged in recent years. These novel viruses proved to be infectious to humans and arose ostensibly through zoonotic jumps from both reservoir species (bats) and amplifier species (raccoon dogs, pangolins). Of these novel coronavirus infections, SARS-CoV2 has proved to be especially worrisome, resulting in a world-wide pandemic and 6.8 million deaths as of March 2023. While mRNA vaccines have curtailed infection and mortality rates, few therapeutic drugs exist for those who do become infected. SARS-CoV2 enters cells by binding its Spike protein to the ACE2 receptor which is expressed in a myriad of tissues, including the lungs and epithelial cells that line blood vessels. SARS-CoV2's entrance into cells via the ACE2 receptor is necessary for the virus to be able replicate and cause downstream pathogenic effects.

Stage of Research
The inventors have identified inhibitors of transmembrane serine protease family member II (TMPRSS2), a known mediator of cell entry of pathogenic coronaviruses. TMPRSS2 is co-expressed in the lung with ACE2, the SARS-CoV2 entry receptor. Briefly, TMPRSS2 proteolyzes the SARS-CoV2 Spike protein at specific cleavage sites following Spike protein binding to ACE2. This cleavage event in turn allows for S2 subunit-driven fusion of viral and host cell membranes, facilitating entry of virus RNA into the cell. Animal studies have shown that inhibition of TMPRSS2 abrogates

cellular entry in the lungs of several coronaviruses including MERS and SARS-CoV2. Prior to the filing of this patent, few TMPRSS2 inhibitors have been described in the literature. This invention identifies type II transmembrane serine proteinase (TTSP) inhibitor as a novel therapeutic for SARS-CoV2 infection. Using computationally modeled protein structures and protein ligand interactions, this invention identifies several TTSPs that bind strongly to TMPRSS2.

Stage of Development
Research -

in vivo

Applications

- Potential therapeutic for SARS-CoV2 by abrogating cellular entry of the virus via the ACE2 receptor
- Potential therapeutic for other coronaviruses that utilize the ACE2 receptor for cellular entry

Advantages

- Can be administered in addition to other anti-viral drugs for a compounded effect due to differing mechanisms of action
- Fills an urgent unmet medical need for therapeutics for those with SARS-CoV2 infections

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