Targeting the SARS-CoV-2 Viral-Immune Interaction for COVID-19 Therapy

New and innovative therapeutic approaches for blocking SARS-CoV-2 engagement with immune cells

Technology

This invention by the Wang Lab (NYU Langone Health) describes (1) the identification of novel receptors on myeloid cells used for engagement by SARS-CoV-2 and (2) the development of a novel bispecific anti-spike nanobody as a potential COVID-19 therapeutic. As presented in Lu et al Immunity 2021, the Tweety family member 2 (TTYH2) receptor and several C-type lectins (DC-SIGN, L-SIGN, LSECtin, ASGR1, and CLEC10A) were identified as glycan-dependent binding partners of the SARS-CoV-2 spike. Engagement of these receptors by the virus spike induced robust proinflammatory responses in myeloid cells that correlated with COVID-19 severity. Furthermore, a novel bispecific anti-spike nanobody was generated that blocked both ACE2-mediated infection and myeloid cell receptor-mediated proinflammatory responses. Taken together, this technology describes new and under-appreciated virus-immune interactions that can be therapeutically exploited for the treatment of COVID-19.

Background

SARS-CoV-2, the etiological agent of Coronavirus Disease 2019 (COVID-19), has caused a global pandemic resulting in millions of deaths worldwide. The high morbidity and mortality of COVID-19 is associated with dysregulated immune responses; yet, surprisingly little is known about the mechanisms underlying immunopathogenesis. In addition to pulmonary epithelial cells, SARS-CoV-2 has also been shown to engage immune cell populations (particularly myeloid cells) resulting in robust proinfammatory responses. Interestingly, unlike host epithelial cells, myeloid cells lack the canonical Angiotensin-converting enzyme 2 (ACE2) cellular receptor, as well as, other putative receptors mediating SARS-CoV-2 entry into host cells. These data strongly suggest that SARS-CoV-2 likely engages and/or infects myeloid cells through independent and poorly understood mechanisms for which our current non-prophylactic COVID-19 treatments are insufficient.

Applications

For the treatment of COVID-19, and other viral infections caused by coronaviruses.

Advantages

- **Novel validated targets:** The described receptors are predominantly expressed in myeloid cells and mediate virus engagement leading to proinflammatory responses.
- **Innovative therapeutic approach:** Myeloid receptor-mediated virus engagement is an under-explored therapeutic avenue for COVID-19 treatment.
- **Lead bispecific anti-spike nanobody with ability to block both ACE2- and myeloid receptor-mediated interactions.**

Technology ID

WAN05-01

Category

COVID-19
Life Sciences/Biologics
Life Sciences/Therapeutics/Infectious Disease/Coronavirus
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Intellectual Property

A U.S. non-provisional patent application has been filed covering composition and method of use.

References

1. Jun Wang, PhD, et al. , https://doi.org/10.1016/j.immuni.2021.05.006