Angiotensin-Converting Enzyme 2 (ACE2) Immunoadhesin Microbody

Improved therapeutic approaches for blocking SARS-CoV-2 entry into host cells

Technology

This invention by the Landau Lab describes an improved form of soluble Angiotensin-converting enzyme 2 (ACE2), termed ACE2 “microbody,” in which the ACE2 ectodomain is fused to domain 3 of an immunoglobulin G Fc. As described in Tada et al Cell Rep 2020, the ACE2 microbody potently inhibited entry of SARS-CoV-2 spike pseudotyped virus and live SARS-CoV-2 (in vitro and in mice) and maintained its antiviral activity even after initial binding of the virus to the cell. Furthermore, the ACE2 microbody is as potent as the best monoclonal antibodies and inhibits entry of a panel of ACE2-specific β coronaviruses and maintains full activity against all of the known SARS-CoV-2 D614G spike protein variants. Taken together, the described technology represents an innovative therapeutic for the treatment of infections caused by SARS-CoV-2 or other ACE2-targeting coronaviruses.

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a global pandemic resulting in millions of deaths worldwide. The spike protein of SARS-COV-2 infects host cells primarily through engagement of the ACE2 cell receptor. Monoclonal antibody therapy has proven to be effective at reducing the severity of symptoms but are susceptible to viral escape by viral variants with spike protein mutations that have become increasingly prevalent. Exogenously administered soluble forms of ACE2 have recently been shown to be potent inhibitors of virus entry by competitively binding to the virus spike protein. Furthermore, soluble ACE2 receptor forms have been engineered as immunoglobulin Fc domain fusions (immunoadhesins) to improve protein stability in vivo. Despite encouraging results in clinical trials, current ACE2-Fc immunoadhesins are hindered by potential “enhancement effects” whereby the fused Ig Fc domain interacts with immune cell Fc receptors to facilitate (rather than inhibit) coronavirus infection. Therefore, improved forms of exogenously administered soluble ACE2 are needed to potently inhibit coronavirus entry into host cells.

Applications

For the treatment of COVID-19, and other viral infections caused by ACE2-targeting coronaviruses

Advantages

Technology ID

LAN02-03

Category

COVID-19
Life Sciences/Biologics
Life Sciences/Therapeutics/Infectious Disease/Coronavirus
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- Validated extracellular target The spike protein is a surface-exposed protein conserved amongst coronaviruses known to mediate viral infection
- Improved antiviral activity relative to soluble ACE2 aloneThe described ACE2 microbody shows 10-fold greater inhibitory activity than soluble ACE2 alone and higher potency than current monoclonal antibodies.
- Pan-Coronavirus applicability The described ACE2 microbody blocks entry of multiple ACE2-specific coronaviruses and the SARS-CoV-2 D614G spike protein variant

IP Status

Non-provisional patent application pending

References

1. Nathaniel R. Landau, PhD, et al. , An ACE2 Microbody Containing a Single Immunoglobulin Fc Domain Is a Potent Inhibitor of SARS-CoV-2