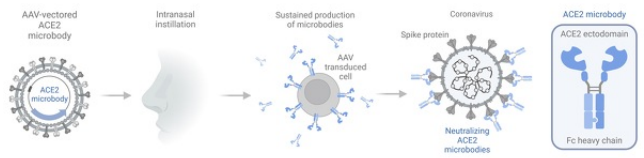
Vectored ACE2 Receptor Decoy for Prevention and Treatment of Pan-Coronavirus Infections

Innovative, alternative, and complementary treatment option for pan-coronavirus infections



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Technology

The Landau Lab has engineered and validated an adeno-associated virus (AAV) vectored microbody comprising a modified Angiotensin-Converting Enzyme 2 (ACE2), which acts as a receptor decoy for the spike protein of coronaviruses, providing long-lasting protection to infection. To enhance efficacy and prevent detrimental side-effects that may result from high exogenous levels of recombinant ACE2, the inventors used only the ectodomain of ACE2 fused to the Fc domain of an immunoglobulin heavy chain, and introduced mutations which both inactivate its catalytic activity and enhance SARS-CoV-2 binding. As shown in proof-of-concept studies (*Tada et al bioRxiv 2023*), the ACE2 AAV vector possesses exceptional functional efficacy when administered intranasaly and intramuscularly, whereby it protects against infection of multiple SARS-CoV-2 variants in both virus-transduced cells and untransduced neighboring cells. In *in vivo* studies, the vectored ACE2 microbody when administered via intranasal instillation potently inhibited viral infection for up to 30 days post treatment. Mice treated prophylactically with the vectored receptor decoy, showed as great as a 100,000-fold decrease in viral load, no histological signs of infection, and no significant loss in body mass. Additionally, when used therapeutically to treat infected mice, the vectored receptor decoy continued to lower viral loads up to 24 hours post infection.

Background

SARS-CoV-2 is a highly contagious coronavirus that causes the respiratory illness known as COVID-19. The disease has rapidly spread worldwide, leading to significant morbidity and mortality, and has had profound impacts on public health, economies, and societies. Despite extensive efforts to develop vaccines and therapeutics, there is still an unmet need for effective treatments to address the ongoing COVID-19 pandemic and future coronavirus pandemics. Currently, the most commonly used treatments for COVID-19 include oxygen therapy, antiviral drugs (remdesivir etc.), and immune modulators (corticosteroids). While these treatments can help alleviate symptoms and improve patient outcomes, they are not universally effectives and carry side effects. The vectored ACE2 receptor decoy technology described herein, offers a promising alternative avenue (vector immunoprophylaxis) for preventing and treating SARS-CoV-2 infections.

Applications

For the treatment of infections caused by SARS-CoV-2 and other coronavirus infections; specifically, in the context of:

- **Prophylaxis:** Protection of high-risk individuals such as healthcare workers, immunocompromised patients, and individuals not vaccinated against coronaviruses.
- **Post-infection treatment:** To establish rapid protection and potentially reduce the severity and duration of the infection.
- **Outbreak containment:** A means to quickly and effectively contain coronavirus outbreaks in nursing homes, hospitals, and other high-risk environments.

Advantages

- **Pan-coronavirus applicability:** By modeling ACE2 in contrast to the viral spike protein, this technology is expected to be effective against all current and future coronaviruses.
- **Specificity:** Targeted administration of the ACE2 AAV and vector tropism provide cell or tissue specific-protection and likely avoid off-target complications.
- **Low toxicity:** The vectored ACE2 receptor decoy does not induce an IFNα, IL-10, TNFα, IL12-p70, IL-6 or MCP-1–mediated inflammatory response.
- **Prophylactic and therapeutic modes of administration:** The ACE2 AAV can confer long-lasting protection pre-infection and establish rapid protection post-infection.
- **Complementarity with existing anti-viral therapies:** The vectored ACE2 receptor decoy could likely be used in combination with other anti-viral treatments to enhance their efficacy or reduce the risk of viral resistance.
- **Alternative coronavirus treatment method:** Individuals who are immunocompromised and at risk from vaccination would benefit this therapy.

Intellectual Property

NYU has filed a provisional patent application covering composition and method of use.

References

1. Takuya Tada, Belinda M. Dcosta, Julia Minnee, Nathaniel R. Landau(2023) , https://doi.org/10.1101/2023.01.11.523649