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TRSbait – RNA-mimicry of viral transcription regulator as antiviral drug

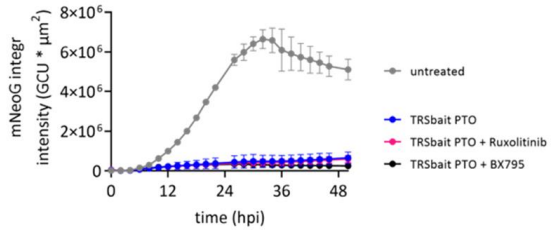
Keywords: Antivirals, SARS-CoV-2, transcriptional regulatory sequences (TRS), RNA-dependent RNA polymerase (RdRp)

INVENTION NOVELTY

Nidovirales, which include the Coronaviridae family, contain specific RNA sequences known as transcriptional regulatory sequences (TRS), which are highly conserved. The 5' leader TRS serves as an initial connection point for the viral RNA-dependent RNA polymerase (RdRp), initiating the transcription of viral RNA.
The concept behind this innovation is to provide a "bait" for the TRS-binding site of the RdRp. Both the TRSbait and the viral TRS compete for binding to the RdRp's TRS-binding site. The TRSbait is provided as an RNA oligonucleotide in high abundance. It saturates the RdRp-TRS-binding site, preventing viral TRS from binding and thereby reducing or even inhibiting viral transcription.

VALUE PROPOSITION

The use of TRSbait with a highly conserved sequence represented in the entire nidoviral family offers several advantages:
Broad applicability: Since TRSbait targets a highly conserved sequence, it can be effective against various viruses within the nidoviral family. This makes it a versatile tool for combating different viral strains. Cost-effectiveness: Oligonucleotides are relatively inexpensive to produce compared to other antiviral treatments, making them a cost-effective option for widespread use. Stability: The phosphorothioate modification (PTO) enhances the stability of the oligonucleotide, making it more resistant to degradation and increasing its lifespan, which is crucial for its effectiveness as a therapeutic agent. Cellular uptake: TRSbait can be delivered into cells using a variety of nucleic acid transfection methods, ensuring efficient delivery to the target site, facilitating interaction with viral RdRp, and effectively disrupting viral transcription. Adaptability: Similar to other RNA-based innovations, TRSbait can be easily modified by sequence changes, enabling swift responses to future pathogenic viruses that utilize TRS sites. In summary, TRSbait's broad specificity, affordability, stability, efficient cellular uptake and flexibility make it a promising candidate for antiviral therapy against the nidoviral family, including coronaviruses and other related viruses.



Anti-SARS-CoV-2 effect of TRSbait. *A549-TA cells transfected with 5 µM of TRSbait were infected with recombinant mNeonGreen-expressing SARS-CoV-2 (icSCV2-mNG). Integrated intensity of the green fluorescent signal over time upon co-treatment with Ruxolitinib (Jak-inhibitor) or BX795 (IKKe-inhibitor). © HZI*

TECHNOLOGY DESCRIPTION

TRSbait is an ssRNA oligonucleotide with a PTO backbone that can be efficiently delivered into cells using conventional transfection methods like lipofection or lipo-nanoparticles, similar to those used in current mRNA vaccine formulations by BioNTech and Moderna. Due to its 24-nucleotide length, the likelihood of escape variants is significantly reduced compared to other drug designs currently in use.

COMMERCIAL OPPORTUNITY

The technology is available for in-licensing and co-development.

DEVELOPMENT STATUS

In vitro tests in A549-TA cells showed that TRSbait treatment represses SARS-CoV-2 infection to the limit of detection.

PATENT SITUATION

A European patent application was filed in February 2023.

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