SARS-CoV-1 gRNA:RTC:nascent RNA minus strand binds RTC inhibitors

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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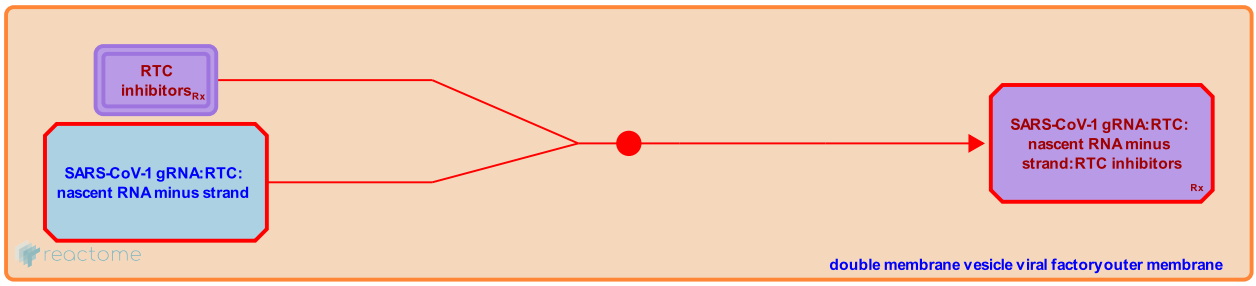
Stable identifier: R-HSA-9687388

Type: binding

Compartments: double membrane vesicle viral factory outer membrane

Diseases: severe acute respiratory syndrome



Remdesivir (GS-5734) is an investigational nucleotide analogue drug that was developed for its broad spectrum antiviral potential against Ebola and Marburg virus activity (Siegel et al. 2017). It targets and inhibits viral RNA-dependent RNA polymerase (nsp12, RdRP), the key component of the replication transcription complex (RTC) (Agostini et al. 2018, Brown et al. 2019, Gordon et al. 2020). Remdesivir is being investigated for potential antiviral activity against SARS-CoV-2 by targeting viral replication (Agostini et al. 2018). Gordon et al. demonstrate remdesivir possesses broad antiviral activity against RNA viruses, including SARS-CoV, MERS-CoV and SARS-CoV-2 in-vitro (Gordon et al. 2020b). It could prevent asymptomatic, mild or moderate COVID-19 cases from progressing to severe disease (clinical trials NCT04252664, NCT04257656) but results so far in infected people have been mixed.

Molnupiravir (EIDD-2801) is an isopropylester prodrug of the ribonucleoside analogue N4-hydroxycytidine (NHC, EIDD-1931) that shows broad spectrum antiviral activity against various RNA viruses including Ebola, Influenza and CoV (Toots et al. 2019). NHC acts as a competitive alternative substrate for virally encoded RNA-dependent RNA polymerases. NHC was shown to inhibit multiple genetically-distinct Bat-CoV viruses in human primary epithelial cells without affecting cell viability. Prophylactic/therapeutic oral administration of NHC reduced lung titers and prevented acute lung failure in C57B/6 mice infected with CoV. The potency of NHC against multiple coronaviruses, its therapeutic efficacy, and oral bioavailability in vivo, all highlight its potential as an effective antiviral against SARS-CoV-2 and other future zoonotic coronaviruses (Sheahan et al. 2020). The clinical trial NCT04575584 was terminated prematurely for ethical reasons because molnupiravir reached its endpoint of effectiveness against COVID-19.

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Editions

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