Direct Host Cell Membrane Membrane Fusion and Release of SARS-CoV-2 Nucleocapsid

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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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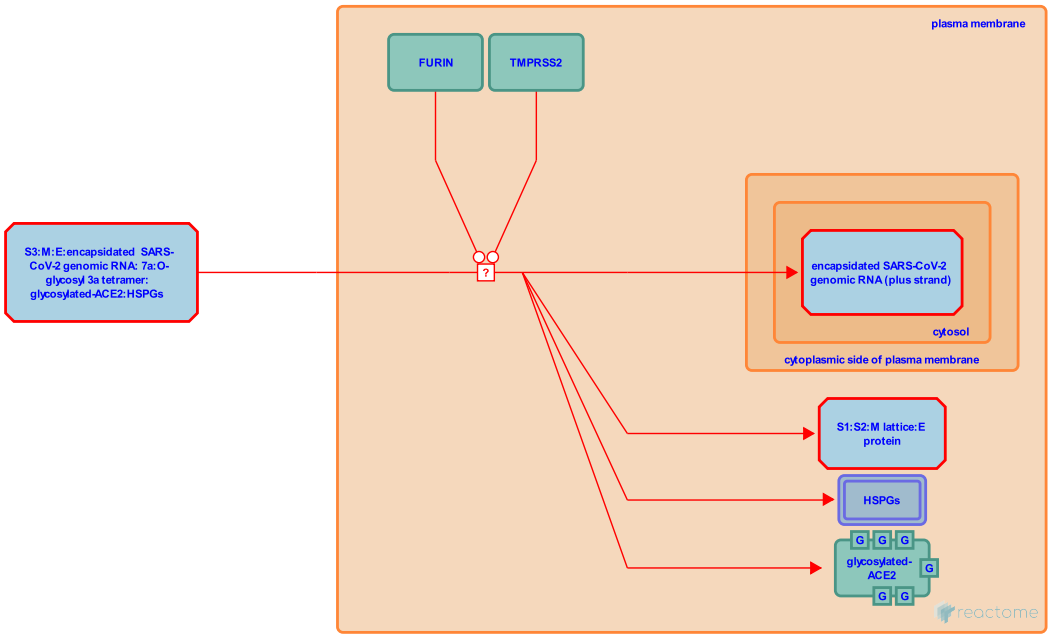
Stable identifier: R-HSA-9698988

Type: uncertain

Compartments: plasma membrane

Diseases: COVID-19



SARS-CoV-2 virions attached to the host cell surface via a complex involving viral spike (S) protein and host angiotensin-converting enzyme 2 (ACE2) can directly fuse their membrane with the host cell membrane, releasing the uncoated virion nucleocapsid into the cytoplasm. The process starts with the spike protein undergoing cleavage by furin into S1/S2, followed by cleavage of S2 catalyzed by TMPRSS2, freeing the fusion peptide (FP) which mediates membrane fusion. Heparin binding to SARS-CoV-2 spike (S) effectively inhibits its cleavage into S1, S2 by furin. Unfractionated heparin (UFH) exhibits a higher furin inhibitory potency than the low-molecular-weight heparin (LMWH) (Paiardi et al, 2021). However, cleavage at the S1/S2 site occurs to some extent even if furin is absent, presumably due to the action of other proprotein convertases (Papa et al, 2021; Jaimes et al, 2020; reviewed by Takeda, 2022).

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Editions

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