

Endocytosis of SARS-CoV-2 Virion

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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

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 77

This document contains 1 reaction ([see Table of Contents](#))

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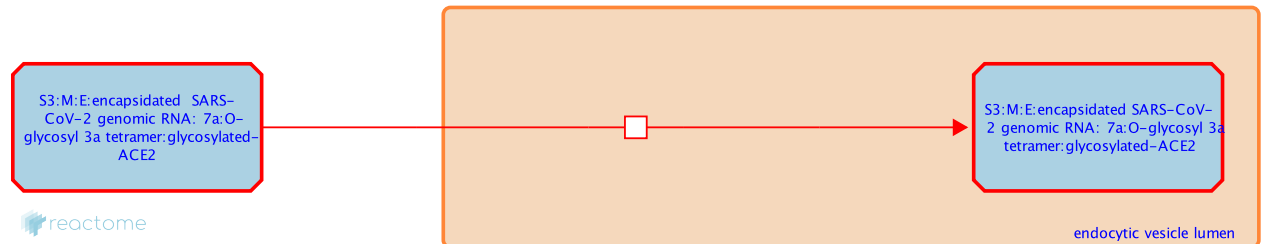
Stable identifier: R-HSA-9697423

Type: transition

Compartments: endocytic vesicle lumen

Diseases: COVID-19

Inferred from: Endocytosis of SARS-CoV-1 Virion (Homo sapiens)



This COVID-19 pathway has been created by a combination of computational inference from SARS-CoV-1 data (<https://reactome.org/documentation/inferred-events>) and manual curation, as described in the summation for the overall SARS-CoV-2 infection pathway.

Based on SARS-CoV-1 experiments, 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) are inferred to undergo endocytosis. In the case of SARS-CoV-1, studies with pseudoviruses have established that S protein is necessary and sufficient for mediating viral attachment and entry. Inhibition of this SARS-CoV-1 S protein-mediated transduction by two different classes of lysosomotropic agents in multiple cell lines strongly suggests that acidification of endosomes is needed for viral entry (Hofmann et al. 2004; Simmons et al. 2004; Yang et al. 2004). The roles of S protein in viral binding to the host cell membrane and fusion of viral and host cell membranes and thus the central role of S protein in determining the host range and tissue tropisms of the virus are reviewed by Belouzard et al. (2012).

Literature references

- Belouzard, S., Millet, JK., Licitra, BN., Whittaker, GR. (2012). Mechanisms of coronavirus cell entry mediated by the viral spike protein. *Viruses*, 4, 1011-33. ↗
- Simmons, G., Reeves, JD., Rennekamp, AJ., Amberg, SM., Piefer, AJ., Bates, P. (2004). Characterization of severe acute respiratory syndrome-associated coronavirus (SARS-CoV) spike glycoprotein-mediated viral entry. *Proc. Natl. Acad. Sci. U.S.A.*, 101, 4240-5. ↗
- Yang, ZY., Huang, Y., Ganesh, L., Leung, K., Kong, WP., Schwartz, O. et al. (2004). pH-dependent entry of severe acute respiratory syndrome coronavirus is mediated by the spike glycoprotein and enhanced by dendritic cell transfer through DC-SIGN. *J. Virol.*, 78, 5642-50. ↗
- Hofmann, H., Hattermann, K., Marzi, A., Gramberg, T., Geier, M., Krumbiegel, M. et al. (2004). S protein of severe acute respiratory syndrome-associated coronavirus mediates entry into hepatoma cell lines and is targeted by neutralizing antibodies in infected patients. *J. Virol.*, 78, 6134-42. ↗

Editions

2020-09-05	Edited	Gillespie, ME.
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