Synthesis of SARS-CoV-2 minus strand sub-genomic mRNAs by template switching

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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. ↗

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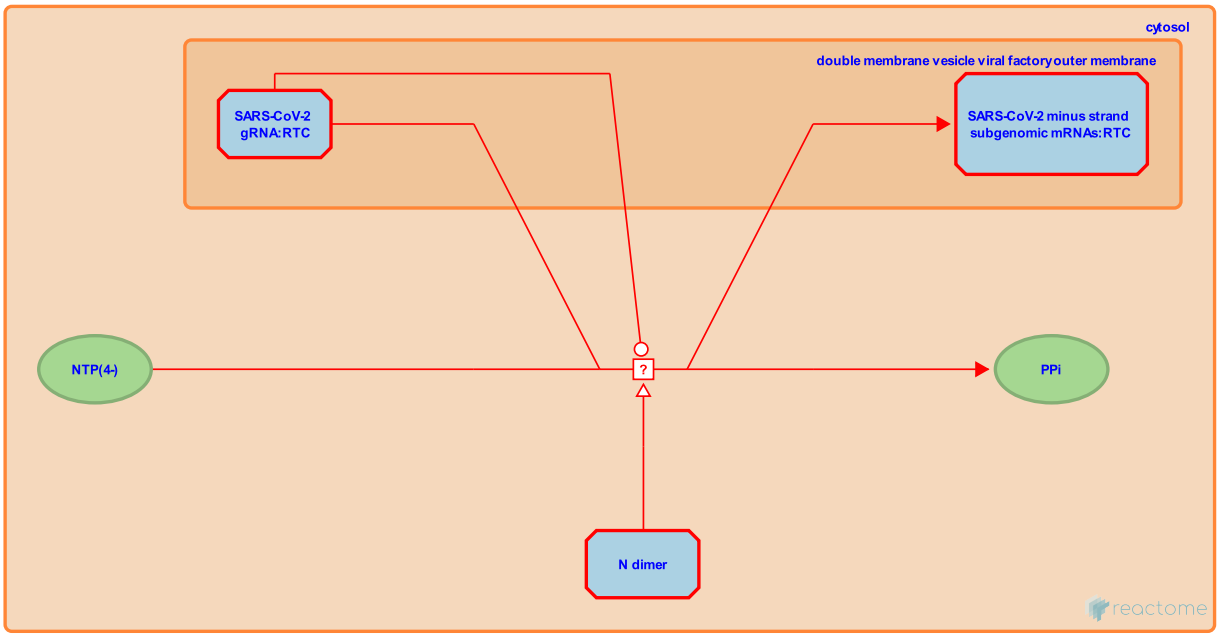
Stable identifier: R-HSA-9694344

Type: uncertain

Compartments: cytosol, double membrane vesicle viral factory outer membrane

Diseases: COVID-19

Inferred from: Synthesis of SARS-CoV-1 minus strand subgenomic mRNAs by template switching (Homo sapiens)



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

SARS-CoV-1 encodes eight subgenomic RNAs, mRNA2 to mRNA9. mRNA1 corresponds to the genomic RNA. The 5' and 3' ends of subgenomic RNAs are identical, in accordance with the template switch model of coronavirus RNA transcription (Snijder et al. 2003, Thiel et al. 2003, Yount et al. 2003). Therefore, consistent with this and the studies of the murine hepatitis virus (MHV), which is closely related to SARS-CoV-1, genomic positive strand RNA is first transcribed into negative sense (minus strand) subgenomic mRNAs, that subsequently serve as templates for the synthesis of positive strand subgenomic mRNAs. Negative-sense virus RNAs are present in much smaller amounts than positive-sense RNAs (Irigoyen et al. 2016). Each subgenomic RNA contains a leader transcription regulatory sequence (leader TRS) that is identical to the leader of the genome, appended via polymerase “jumping” during negative strand synthesis to the body transcription regulatory sequence (body TRS), a short, AU-rich motif of about 10 nucleotides found upstream of each ORF that is destined to become 5' proximal in one of the subgenome-length mRNAs. The 3' and 5'UTRs may interact through RNA–RNA and/or RNA–protein plus protein–protein interactions to promote circularization of the coronavirus genome, placing the elongating minus strand in a favorable topology for leader-body joining. The host protein PABP was found to bind to the coronavirus 3' poly(A) tail and to interact with the host protein eIF-4G, a component of the three-subunit complex that binds to mRNA cap structures, which may promote the circularization of the coronavirus genome. Two viral proteins that bind to the coronavirus 5'UTR, the N protein and nsp1, may play a role in template switching. The poly(A) tail is necessary for the initiation of minus-strand RNA synthesis at the 3' end of genomic RNA. For review, please refer to Sawicki et al. 2007 and Yang and Leibowitz 2015.

Editions

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