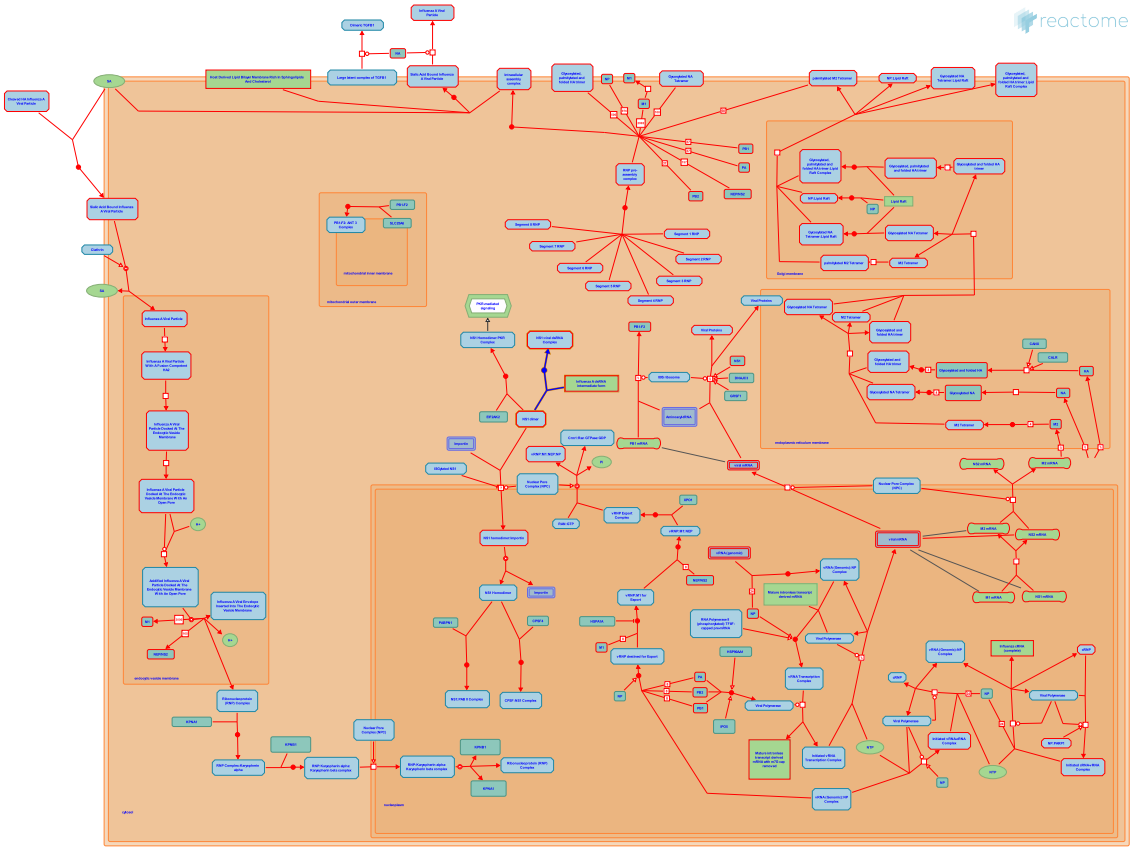
Inhibition of IFN-beta



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

21/05/2024

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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

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. ↗

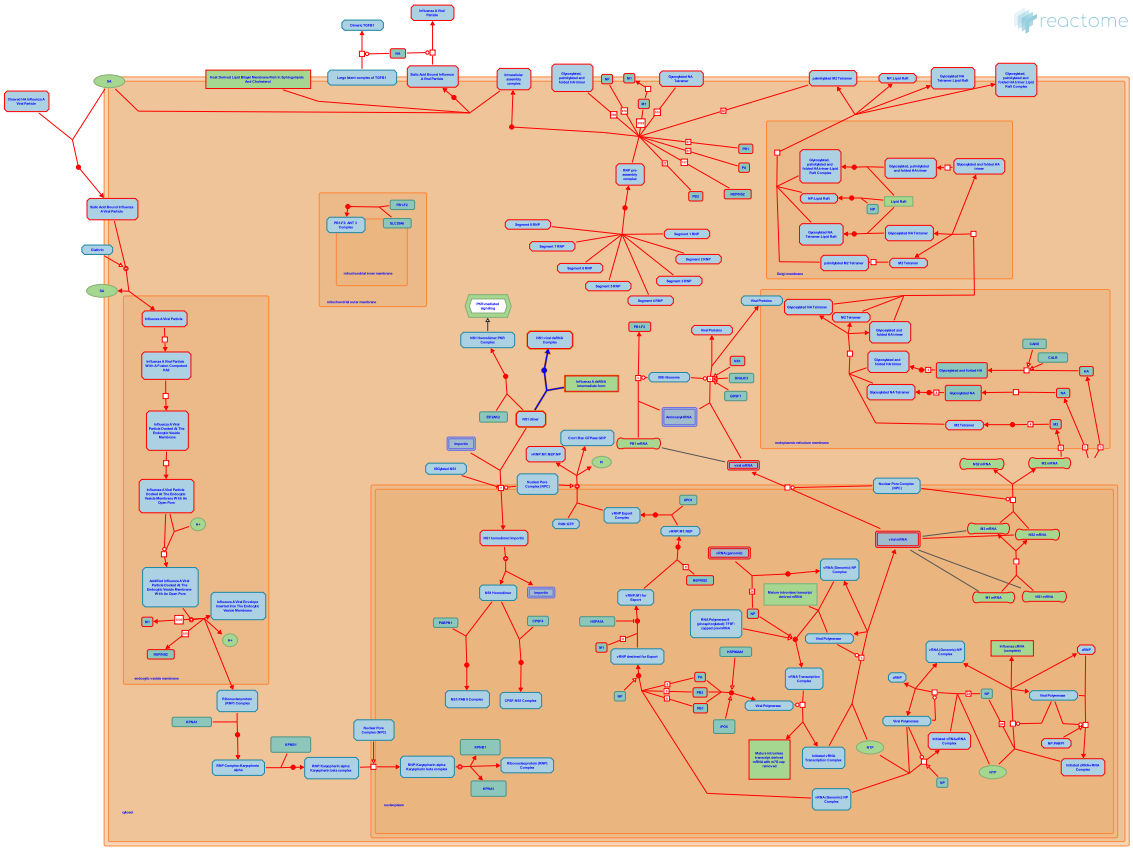
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Inhibition of IFN-beta ↗

Stable identifier: R-HSA-168888

Diseases: influenza



Since the presence of intracellular dsRNA serves as the signal for virus infection and triggers host interferon (IFN) synthesis the simplest model for viral NS1 protein function is that it sequesters dsRNA and thus prevents the downstream signaling required to activate IRF-3, NF-kB and AP-1. These findings are strongly supported by mutational analyses of NS1 that indicate that the IFN antagonist properties of NS1 depend on its ability to bind dsRNA. However, a compensatory mutation (S42G), which was acquired during the passaging of the mutant RNA-binding virus, results in partial restoration of wild-type phenotype but does not restore RNA binding. This indicates that the ability of NS1 to inhibit IFN synthesis is not solely dependent on dsRNA binding and that additional mechanisms may be involved.

Literature references

Garcia-Sastre, A., Donelan, NR., Basler, CF. (2003). A recombinant influenza A virus expressing an RNA-binding-defective NS1 protein induces high levels of beta interferon and is attenuated in mice. *J Virol, 77*, 13257-66. ↗

Editions

2004-05-12	Reviewed	Gale M, Jr.
2013-11-18	Authored	Gillespie, ME.

Binding of NS1 to dsRNA ↗

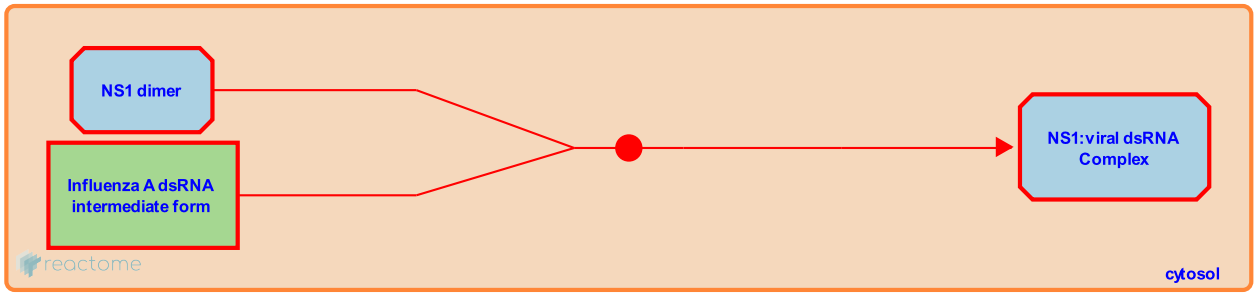
Location: Inhibition of IFN-beta

Stable identifier: R-HSA-168891

Type: binding

Compartments: cytosol

Diseases: influenza



The ability of viral non-structural protein 1 (NS1) to sequester dsRNA is believed to be one of the primary mechanisms by which NS1 prevents activation of downstream anti-viral signaling pathways.

Literature references

Garcia-Sastre, A., Donelan, NR., Basler, CF. (2003). A recombinant influenza A virus expressing an RNA-binding-defective NS1 protein induces high levels of beta interferon and is attenuated in mice. *J Virol, 77*, 13257-66. ↗

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