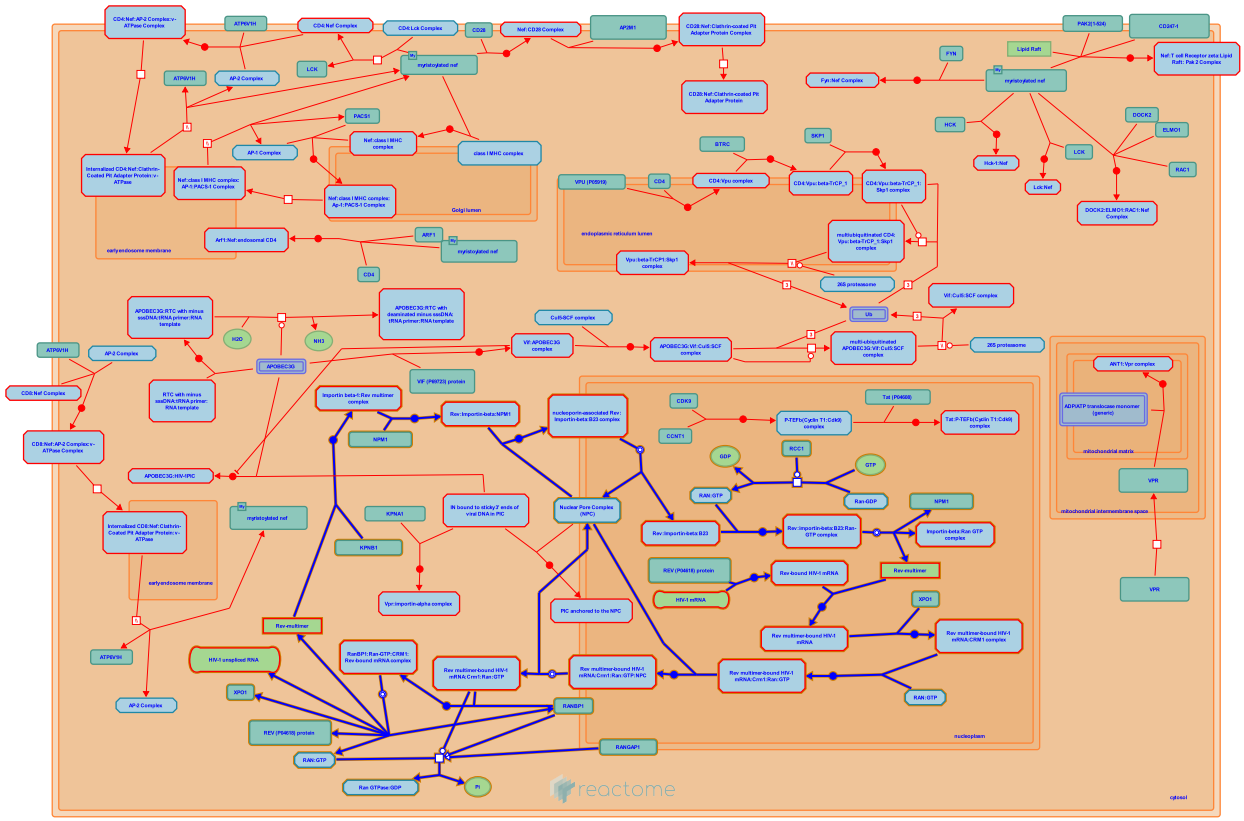
Interactions of Rev with host cellular proteins



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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.

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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.
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. ↗

Reactome database release: 88

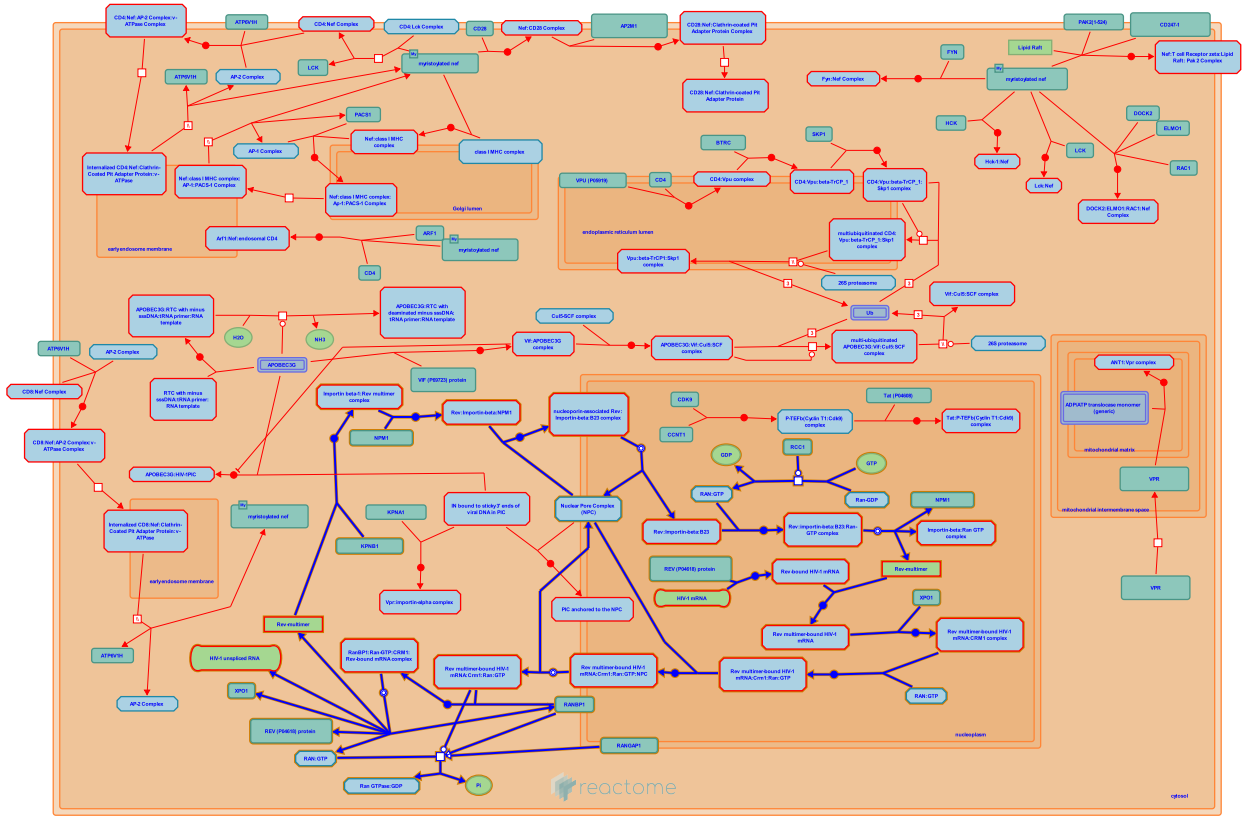
This document contains 3 pathways (see Table of Contents)

Interactions of Rev with host cellular proteins ↗

Stable identifier: R-HSA-177243

Compartments: nucleoplasm

Diseases: Human immunodeficiency virus infectious disease



In order to facilitate the transport of incompletely spliced HIV-1 transcripts, Rev shuttles between the cytoplasm and nucleus using host cell transport mechanisms (reviewed in Li et al. 2005). Nuclear import appears to be achieved by the association of Rev with importin-beta and B23 and docking at the nuclear pore through interactions between importin-beta and nucleoporins. The dissociation of Rev with the import machinery and the subsequent export of Rev-associated HIV-1 mRNA complex requires Ran-GTP. Ran GTP associates with importin-beta, displacing its cargo. Crm1 associates with the Rev:RNA complex and Ran:GTP and is believed to interact with nucleoporins facilitating docking of the RRE-Rev-CRM1-RanGTP complex to the nuclear pore and the translocation of the complex across the nuclear pore complex. In the cytoplasm, RanBP1 associates with Ran-GTP causing the Crm1-Rev-Ran-GTP complex to disassemble. The Ran GAP protein promotes the hydrolysis of RanGTP to Ran GDP. The activities of Ran GAP in the cytoplasm and Ran-GEF, which converts RAN-GDP to Ran-GTP in the nucleus, produce a gradient of Ran-GTP/GDP required for this shuttling of Rev and other cellular transport proteins.

Literature references

Jensen, TH., Englmeier, L., Nilsson, J., Askjaer, P., Kjems, J. (1998). The specificity of the CRM1-Rev nuclear export signal interaction is mediated by RanGTP. *J Biol Chem, 273*, 33414-22. ↗

Editions

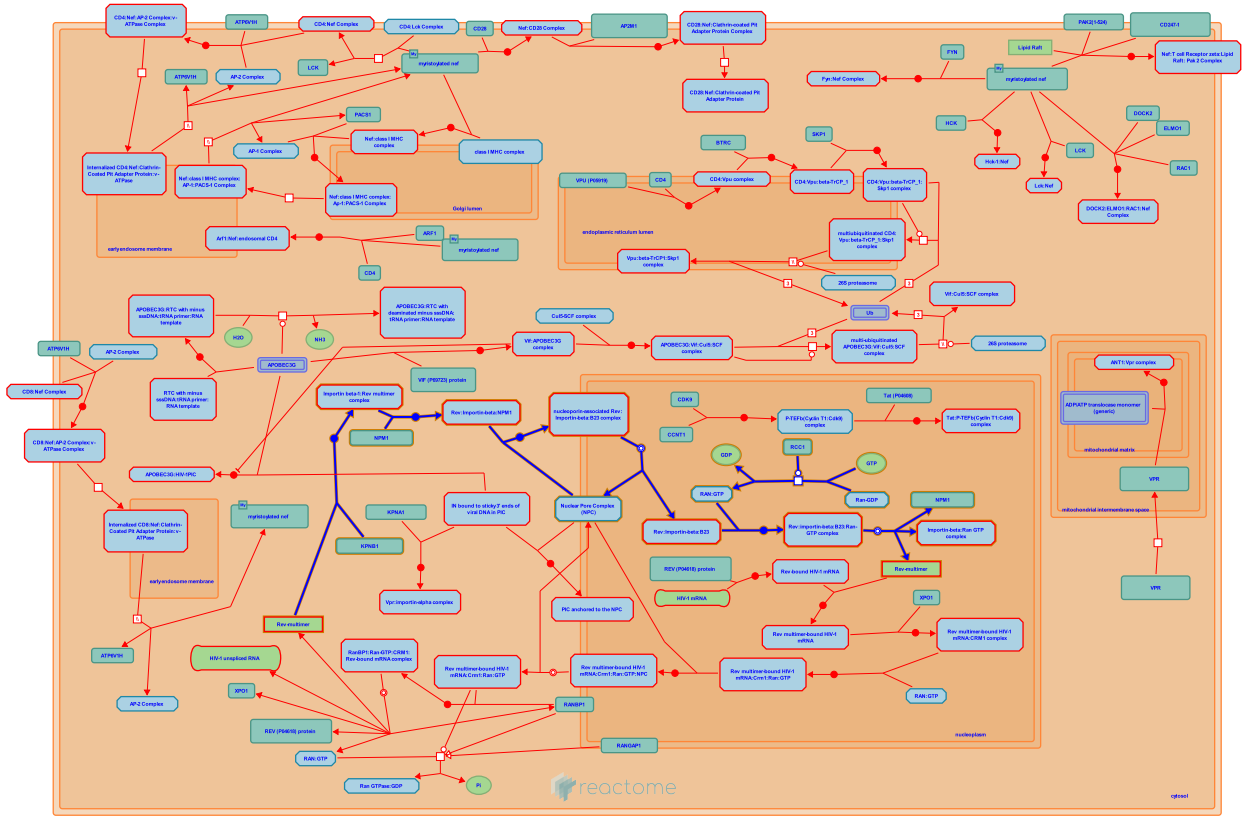
2005-07-27	Authored	Matthews, L., Rice, AP.
2006-03-24	Edited	Matthews, L.
2007-02-01	Reviewed	Kumar, A.

Nuclear import of Rev protein ↗

Location: Interactions of Rev with host cellular proteins

Stable identifier: R-HSA-180746

Diseases: Human immunodeficiency virus infectious disease



Nuclear import of Rev involves the cellular proteins including importin-beta and B23 and is mediated by an arginine-rich nuclear localization signal (NLS) within the RNA binding domain of the Rev protein. The NLS of Rev associates with importin- beta as well as B23 which has been shown to function in the nuclear import of ribosomal proteins. The Rev-importin beta-B23 complex associates with the nuclear pore through interactions between importin beta and nucleoporin. Upon entry into the nucleus, Ran-GTP associates with importin beta resulting in in the disassembly of the importin beta-Rev-B23 complex and the release of Rev cargo.

Editions

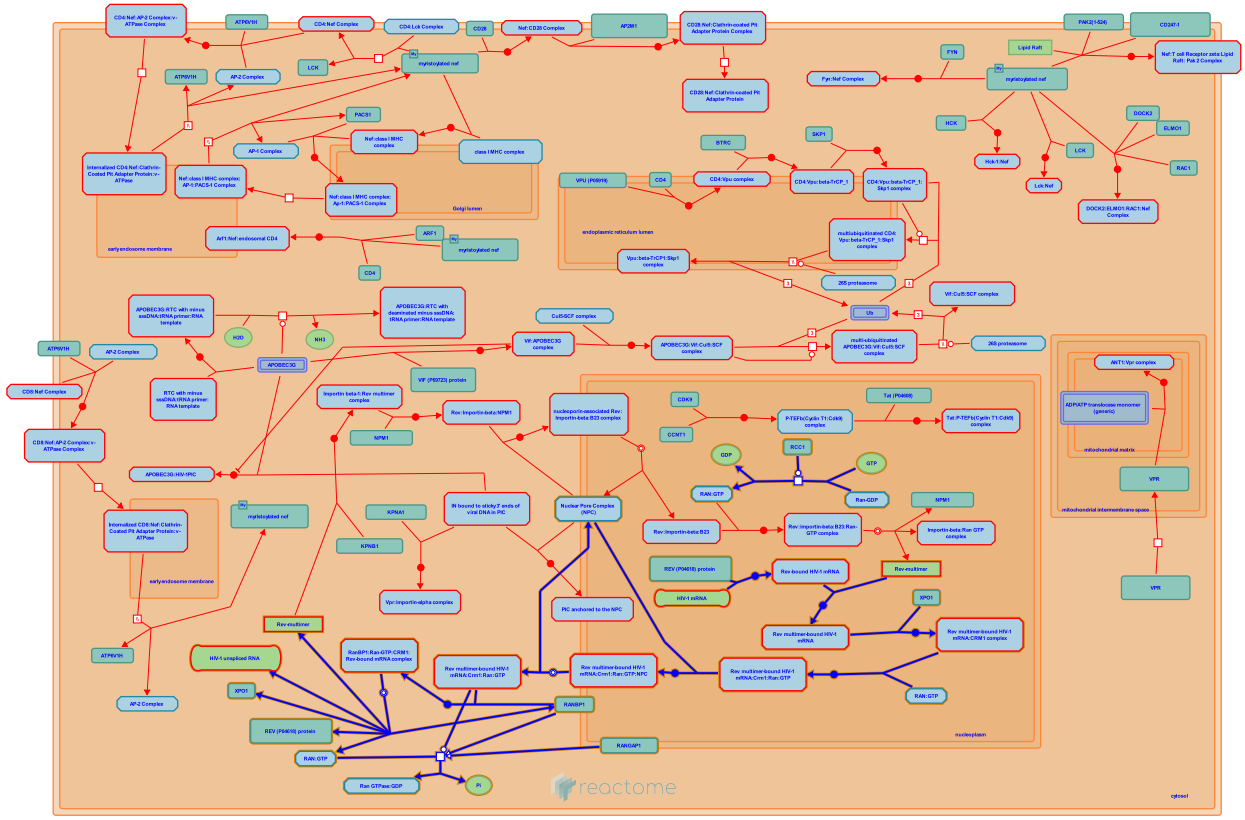
2006-06-08	Authored	Matthews, L.
2007-02-01	Reviewed	Kumar, A.
2007-02-01	Edited	Matthews, L.

Rev-mediated nuclear export of HIV RNA ↗

Location: Interactions of Rev with host cellular proteins

Stable identifier: R-HSA-165054

Diseases: Human immunodeficiency virus infectious disease



The HIV-1 genome contains 9 genes encoded by a single transcript. In order for the virus to replicate, unspliced, singly-spliced and fully spliced viral mRNA must be exported from the nucleus. The HIV-1 mRNA splice sites are inefficient resulting it the accumulation of a pool of incompletely spliced RNAs (Staffa and Cochrane, 1994). In the early stages of the viral life cycle, or in the absence of the viral Rev protein, completely spliced viral mRNA which encode the regulatory proteins Tat, Nef and Rev are exported from the nucleus while the incompletely spliced structural protein encoding transcripts are held within the nucleus by cellular proteins that normally function in preventing the nuclear export of cellular pre-mRNA. Export of both unspliced and partially spliced mRNA is mediated by the viral protein Rev which is recruited, along with cellular cofactors, to the Rev Response Element (RRE) within the HIV-1 mRNA sequence (Malim et al., 1990; Fischer et al., 1994). The cellular hRIP protein is essential for correct Rev-mediated export of viral RNAs to the cytoplasm (Sanchez-Velar et al., 2004; Yu et al., 2005).

Literature references

Green, MR., Fritz, CC. (1996). HIV Rev uses a conserved cellular protein export pathway for the nucleocytoplasmic transport of viral RNAs. *Curr Biol, 6*, 848-54. ↗

Cullen, BR. (1998). Retroviruses as model systems for the study of nuclear RNA export. *Virology, 249*, 203-10. ↗

Cullen, BR. (2003). Nuclear mRNA export: insights from virology. *Trends Biochem Sci, 28*, 419-24. ↗

Editions

2005-07-27	Authored	Matthews, L., Rice, AP.
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2007-02-01	Reviewed	Kumar, A.

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