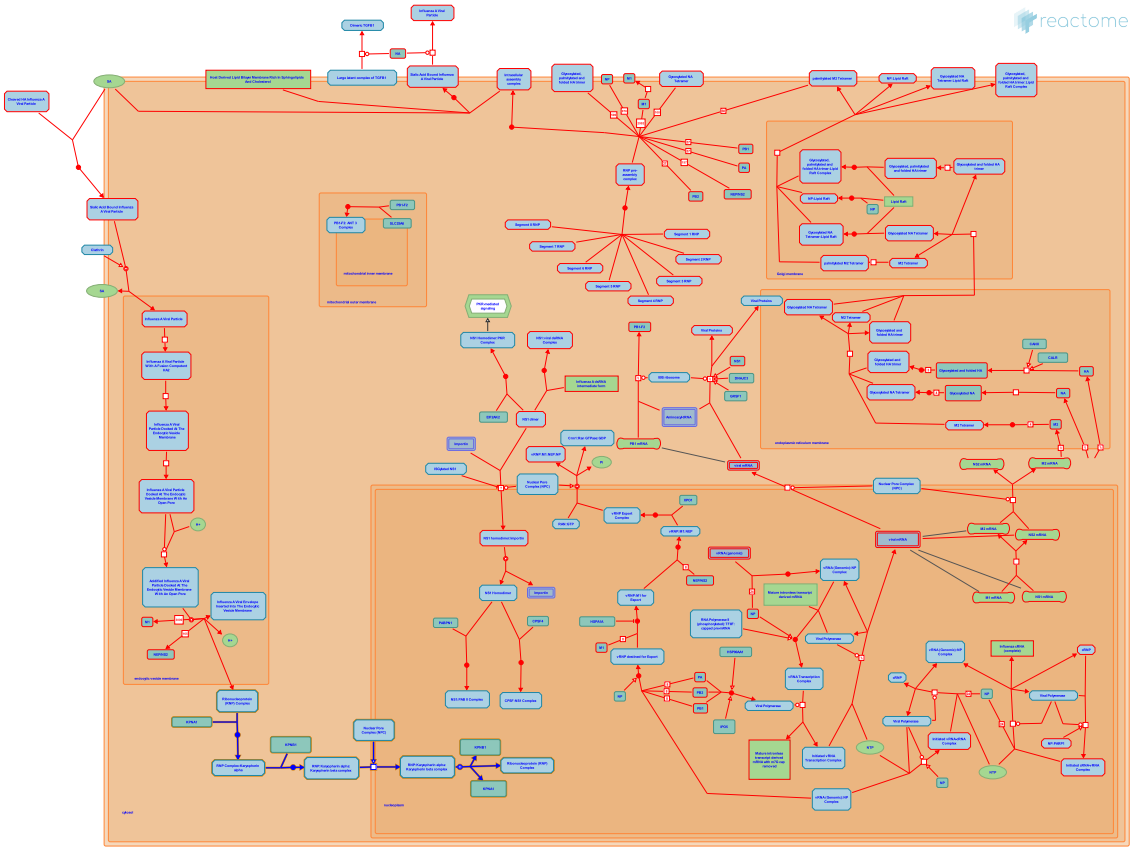
Transport of Ribonucleoproteins into the Host Nucleus



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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. ↗

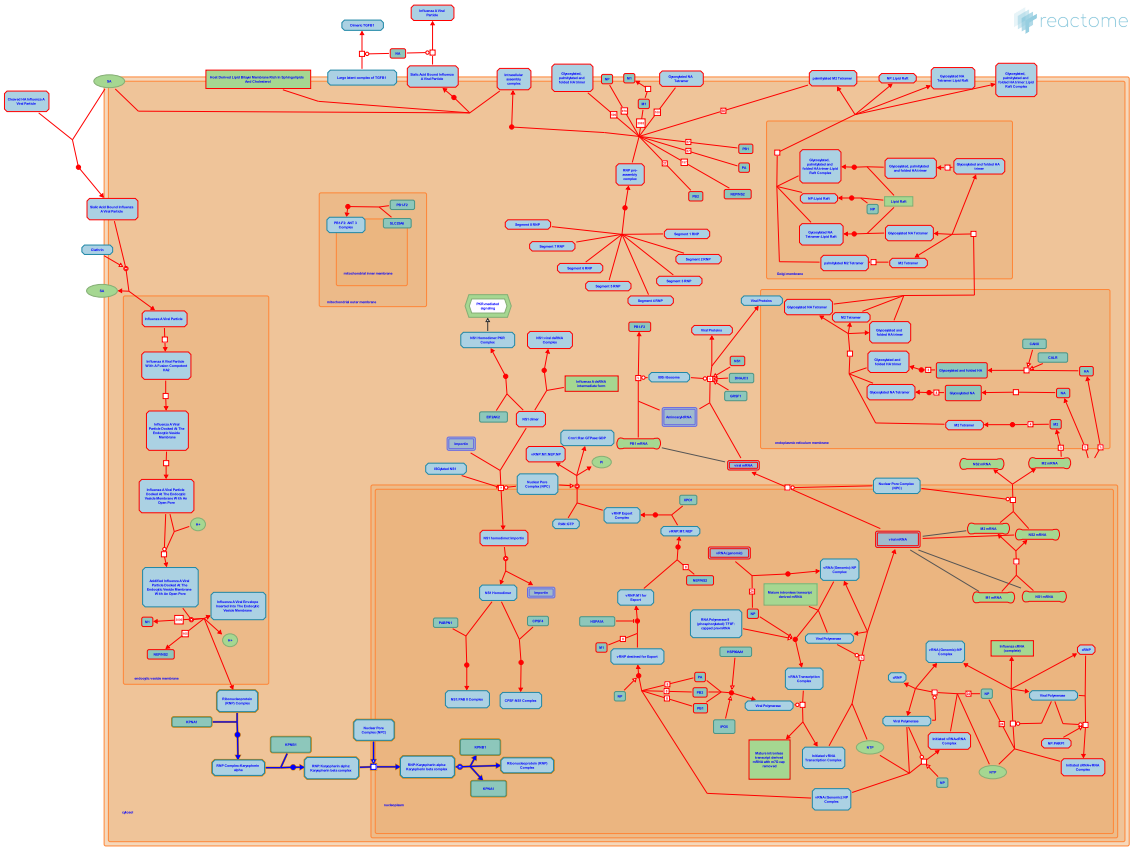
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Transport of Ribonucleoproteins into the Host Nucleus ↗

Stable identifier: R-HSA-168271

Diseases: influenza



An unusual characteristic of the influenza virus life cycle is its dependence on the nucleus. Trafficking of the viral genome into and out of the nucleus is a tightly regulated process with all viral RNA synthesis occurring in the nucleus. The eight influenza virus genome segments never exist as naked RNA but are associated with four viral proteins to form viral ribonucleoprotein complexes (vRNPs). The major viral protein in the RNP complex is the nucleocapsid protein (NP), which coats the RNA. The remaining proteins PB1, PB2 and PA bind to the partially complementary ends of the viral RNA, creating the distinctive panhandle structure. These RNPs (10-20nm wide) are too large to passively diffuse into the nucleus and therefore, once released from an incoming particle must rely on the active import mechanism of the host cell nuclear pore complex. All proteins in the RNP complex can independently localize to the nucleus due to the presence of nuclear localization signals (NLSs) which mediate their interaction with the nuclear import machinery, including the RanGTPase (Fodor, 2004; Deng et al., 2006). However the signals on NP have been shown to be both sufficient and necessary for the import of viral RNA.

Literature references

Shaw, ML., Palese, P. (2001). Orthomyxoviridae: The Viruses and Their Replication. *Fields Virology, 5th edition D.M. Knipe and P.M. Howley, Editors. 2006, Lippencott Williams and Wilkins: Philadelphia ISBN-10: 0-7817-6060-7*, 1647-1689. ↗

Editions

2005-11-14	Authored	Gillespie, ME.
2006-10-29	Reviewed	Squires, B.

Recognition of the Nuclear Localization Signal (NLS) by a Karyopherin Alpha Family Protein ↗

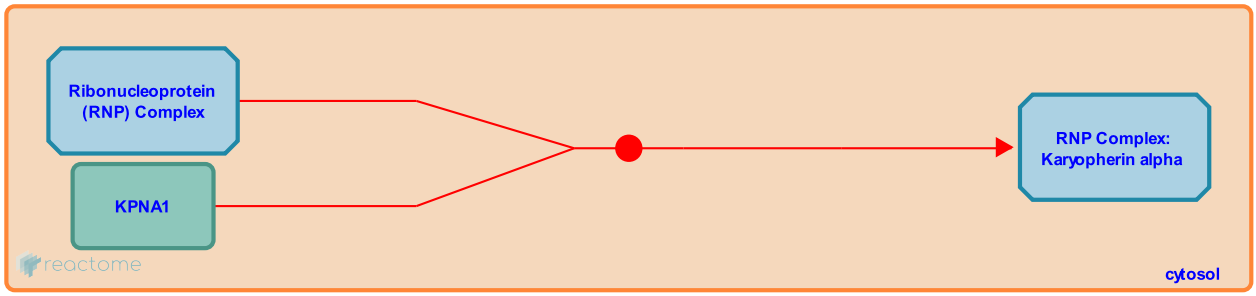
Location: Transport of Ribonucleoproteins into the Host Nucleus

Stable identifier: R-HSA-168297

Type: binding

Compartments: cytosol

Diseases: influenza



The eight influenza virus genome segments never exist as naked RNA but are associated with four viral proteins to form viral ribonucleoprotein complexes (vRNPs). The major viral protein in the RNP complex is the nucleocapsid protein (NP), which coats the RNA. The remaining proteins PB1, PB2 and PA bind to the partially complementary ends of the viral RNA, creating the distinctive panhandle structure. The influenza viral NP behaves like a nuclear localization sequence (NLS) containing protein. The RNP docks at the nuclear envelope only in the presence of the heterodimeric karyopherin alpha and beta complex. Here karyopherin alpha recognizes the RNP.

Followed by: Recruitment of Karyopherin Beta to form a Trimeric Complex

Literature references

Garcia-Sastre, A., Palese, P., Cros, JF. (2005). An unconventional NLS is critical for the nuclear import of the influenza A virus nucleoprotein and ribonucleoprotein. *Traffic, 6*, 205-13. ↗

Moroianu, J., Blobel, G., Palese, P., Jaskunas, R., O'Neill, RE. (1995). Nuclear import of influenza virus RNA can be mediated by viral nucleoprotein and transport factors required for protein import. *J Biol Chem, 270*, 22701-4. ↗

Editions

2005-11-14	Authored	Gillespie, ME.
2006-10-29	Reviewed	Squires, B.

Recruitment of Karyopherin Beta to form a Trimeric Complex ↗

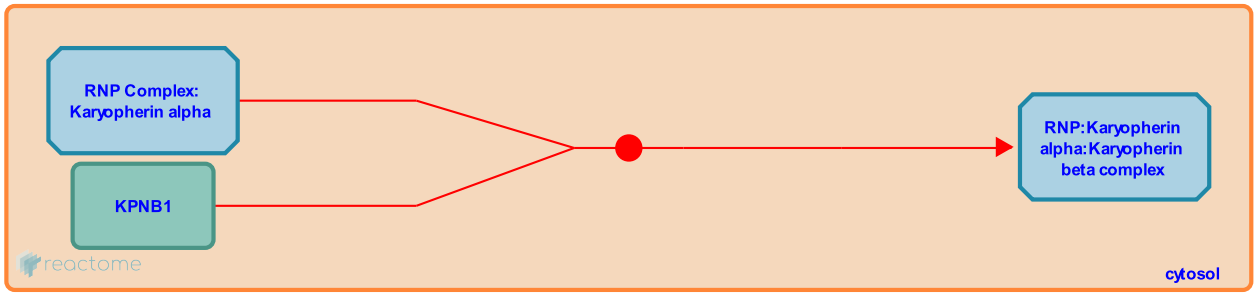
Location: Transport of Ribonucleoproteins into the Host Nucleus

Stable identifier: R-HSA-168317

Type: binding

Compartments: cytosol

Diseases: influenza



The eight influenza virus genome segments are associated with four viral proteins to form viral ribonucleoprotein complexes (vRNPs). The major viral protein in the RNP complex is the nucleocapsid protein (NP), which coats the RNA. The remaining proteins PB1, PB2 and PA bind to the partially complementary ends of the viral RNA. The influenza viral NP behaves like a nuclear localization sequence (NLS) containing protein. The RNP docks at the nuclear envelope only in the presence of the heterodimeric karyopherin alpha and beta complex. Once the NLS is recognized by karyopherin alpha the karyopherin beta subunit joins the complex.

Preceded by: Recognition of the Nuclear Localization Signal (NLS) by a Karyopherin Alpha Family Protein

Followed by: Docking and transport of the RNP:Karyopherin complex through the nuclear pore

Literature references

Moroianu, J., Blobel, G., Palese, P., Jaskunas, R., O'Neill, RE. (1995). Nuclear import of influenza virus RNA can be mediated by viral nucleoprotein and transport factors required for protein import. *J Biol Chem, 270*, 22701-4. ↗

Editions

2005-11-14	Authored	Gillespie, ME.
2006-10-29	Reviewed	Squires, B.

Docking and transport of the RNP:Karyopherin complex through the nuclear pore ↗

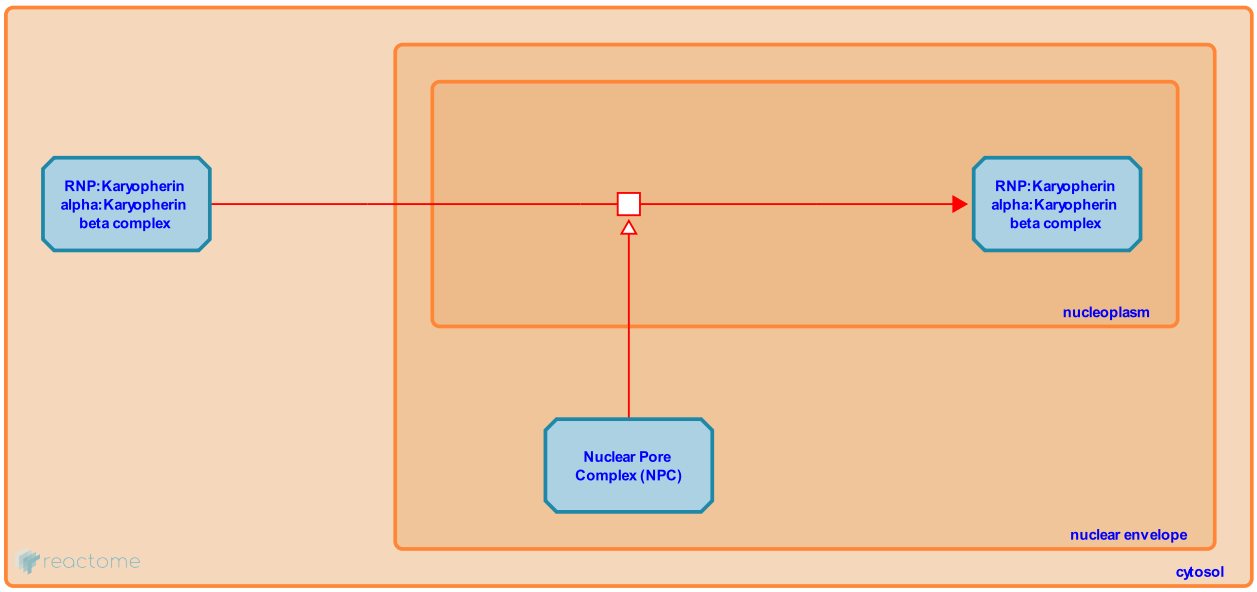
Location: Transport of Ribonucleoproteins into the Host Nucleus

Stable identifier: R-HSA-168337

Type: transition

Compartments: nucleoplasm, cytosol

Diseases: influenza



These RNPs (10-20nm wide) are too large to passively diffuse into the nucleus and therefore, once released from an incoming particle they must rely on the active import mechanism of the host cell nuclear pore complex (NPC). Once the RNP heterodimeric karyopherin complex docks at the NPC, it is transported into the nucleus.

Preceded by: Recruitment of Karyopherin Beta to form a Trimeric Complex

Followed by: Release of the RNP into the host cell nucleus

Literature references

Nayak, DP., Mukaigawa, J. (1991). Two signals mediate nuclear localization of influenza virus (A/WSN/33) polymerase basic protein 2. *J Virol, 65*, 245-53. ↗

Editions

2005-11-14	Authored	Gillespie, ME.
2006-10-29	Reviewed	Squires, B.

Release of the RNP into the host cell nucleus ↗

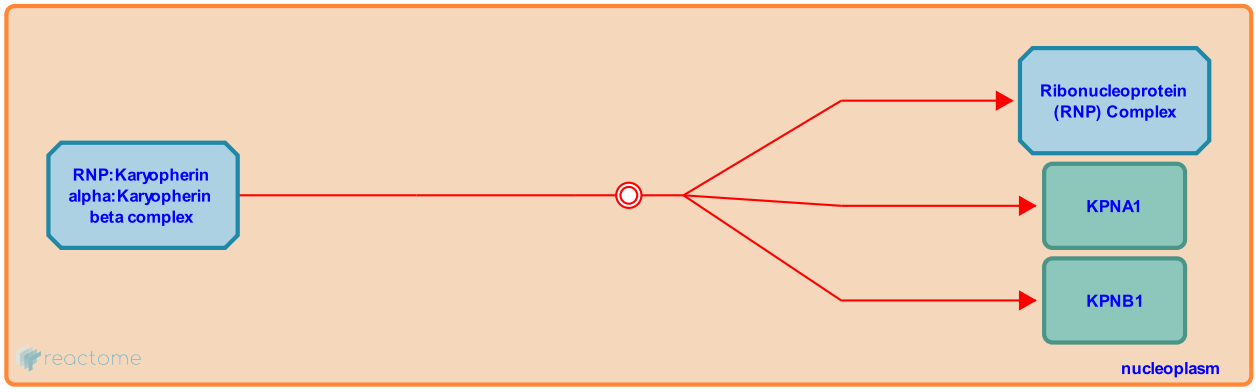
Location: Transport of Ribonucleoproteins into the Host Nucleus

Stable identifier: R-HSA-168310

Type: dissociation

Compartments: nucleoplasm

Diseases: influenza



Once the viral RNP and heterodimeric karyopherin complex has been transported into the nucleus the RNP dissasociates from the heterodimeric karyopherins.

Preceded by: Docking and transport of the RNP:Karyopherin complex through the nuclear pore

Literature references

Moroianu, J., Blobel, G., Palese, P., Jaskunas, R., O'Neill, RE. (1995). Nuclear import of influenza virus RNA can be mediated by viral nucleoprotein and transport factors required for protein import. *J Biol Chem, 270*, 22701-4. ↗

Editions

2005-11-14	Authored	Gillespie, ME.
2006-10-29	Reviewed	Squires, B.

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