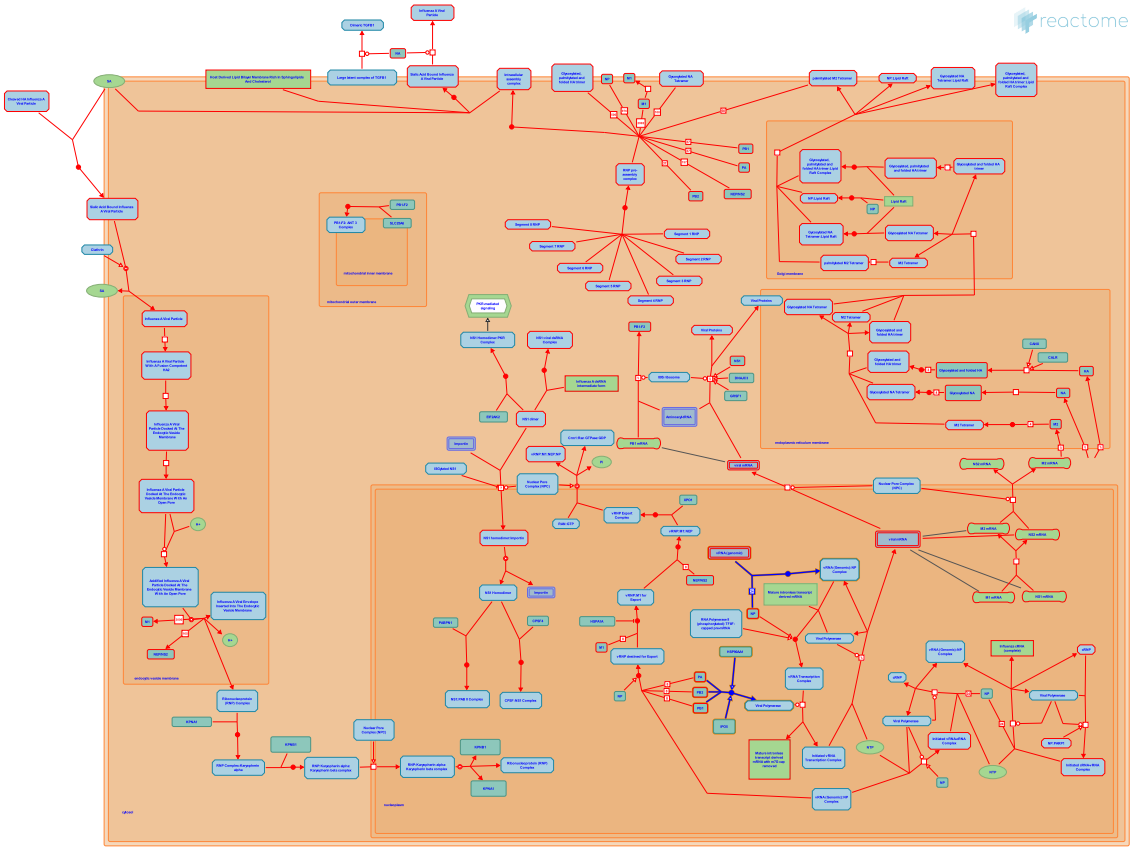
vRNP Assembly



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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).

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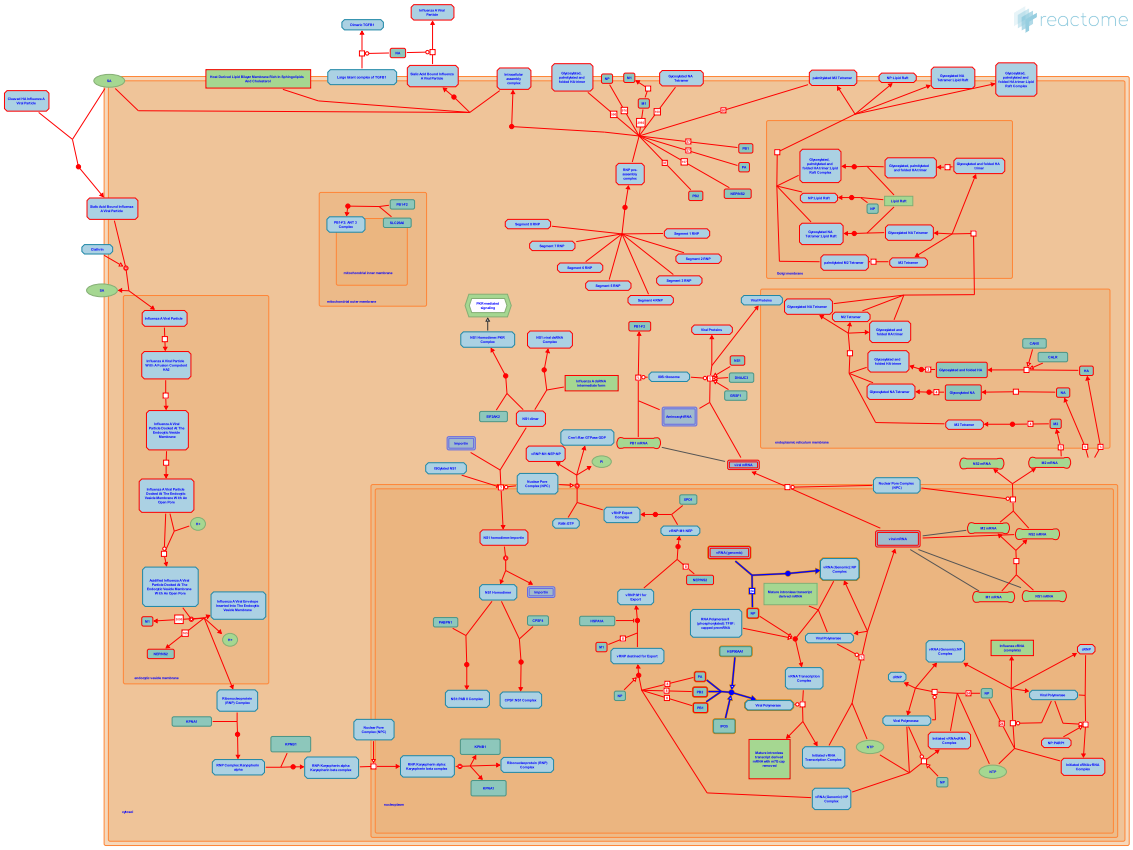
vRNP Assembly ↗

Stable identifier: R-HSA-192905

Compartments: nucleoplasm

Diseases: influenza



For each of eight gene segments, a viral ribonucleoprotein (vRNP), containing a viral negative-sense RNA (vRNA) segment complexed with nucleoprotein (NP) and the trimeric influenza polymerase (PB1, PB2, and PA), is assembled in the nucleus (Braam, 1983; Jones, 1986; Cros, 2003; reviewed in Buolo, 2006). The vRNP functions in three modes (reviewed in Mikulasova, 2000; Neumann, 2004): (1) transcription, which synthesizes viral messenger RNA from the vRNA template using as primers 5' ends of cellular mRNAs containing the cap; (2) replication, which produces positive-sense complementary RNA (cRNA) and subsequently vRNA, both complexed with NP and the trimeric polymerase; or (3), the vRNP is exported from the nucleus into the cytoplasm and is incorporated into assembling virions at the plasma membrane.

Literature references

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Editions

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2007-02-13	Reviewed	Squires, B.

Viral Polymerase Assembly ↗

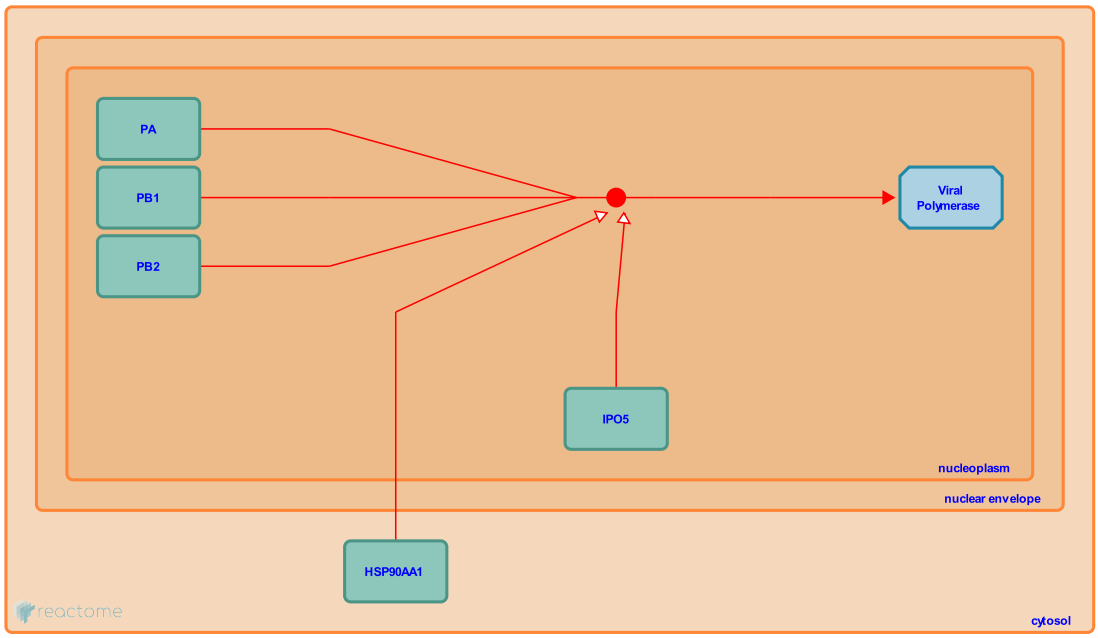
Location: vRNP Assembly

Stable identifier: R-HSA-192830

Type: binding

Compartments: nucleoplasm

Diseases: influenza



The mature ternary influenza viral polymerase complex consists of PB1, PB2, and PA. The N-terminus of PB1 (residues 1-48) interacts with PB2, and amino acids 506-659 in PB1 interact with the PA subunit (Gonzalez, 1996; Perez, 2001). Although monomeric PB1, PB2 and PA, as well as PB1-PB2 and PB1-PA dimers are likely to exist in infected cells, it is believed that most of the polymerase proteins are assembled into the trimeric PB1-PB2-PA complex (Detjen, 1987). Newly synthesized subunits of the polymerase are imported into the nucleus through nuclear localization signals (NLS), which interact with cellular importin family proteins (Jones, 1986; Buolo, 2006). Importin beta-3 (Ran binding protein 5) facilitates nuclear import of PB1 and a PB1-PA dimer (Deng, 2006); coexpression of PA with PB1 was shown to enhance the import of PB1 (Fodor, 2004). A PB1-PB2 dimer has been found to interact with the molecular chaperone heat shock protein 90 (HSP90) to facilitate import (Naito, 2007). The three subunits assembled in the nucleus form a mature ternary polymerase complex that binds viral vRNA or cRNA (Jones, 1986; Buolo, 2006).

Literature references

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NP binds vRNA ↗

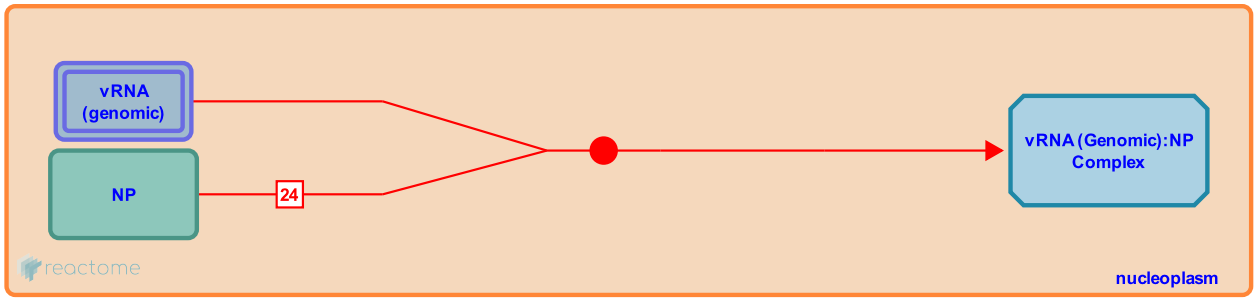
Location: vRNP Assembly

Stable identifier: R-HSA-192912

Type: binding

Compartments: nucleoplasm

Diseases: influenza



Viral genomic RNA (vRNA) and complementary RNA (cRNA) are likely bound by the influenza nucleoprotein (NP) immediately upon synthesis. Although two nuclear localization signals have been mapped in the NP, an unconventional N-terminal NLS and a bipartite NLS within amino acids 198-216 (Wang, 1997; Neumann, 1997; Ozawa, 2007), the crystal structure of the NP suggests that only the unconventional NLS is exposed and can be used as a functional NLS (Ye, 2006). This unconvenetional NLS interacts with importins alpha-1 and -2 (Cros et al., 2005; Wang et al., 1997; Buolo et al., 2006). The three-dimensional structure of NP has revealed that NP molecules associate as a trimer, interacting through beta-sheets b5, b6, and b7 in the C-terminal domain of the protein; the viral RNA likely wraps around the outside of the complex (Ye, 2006).

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