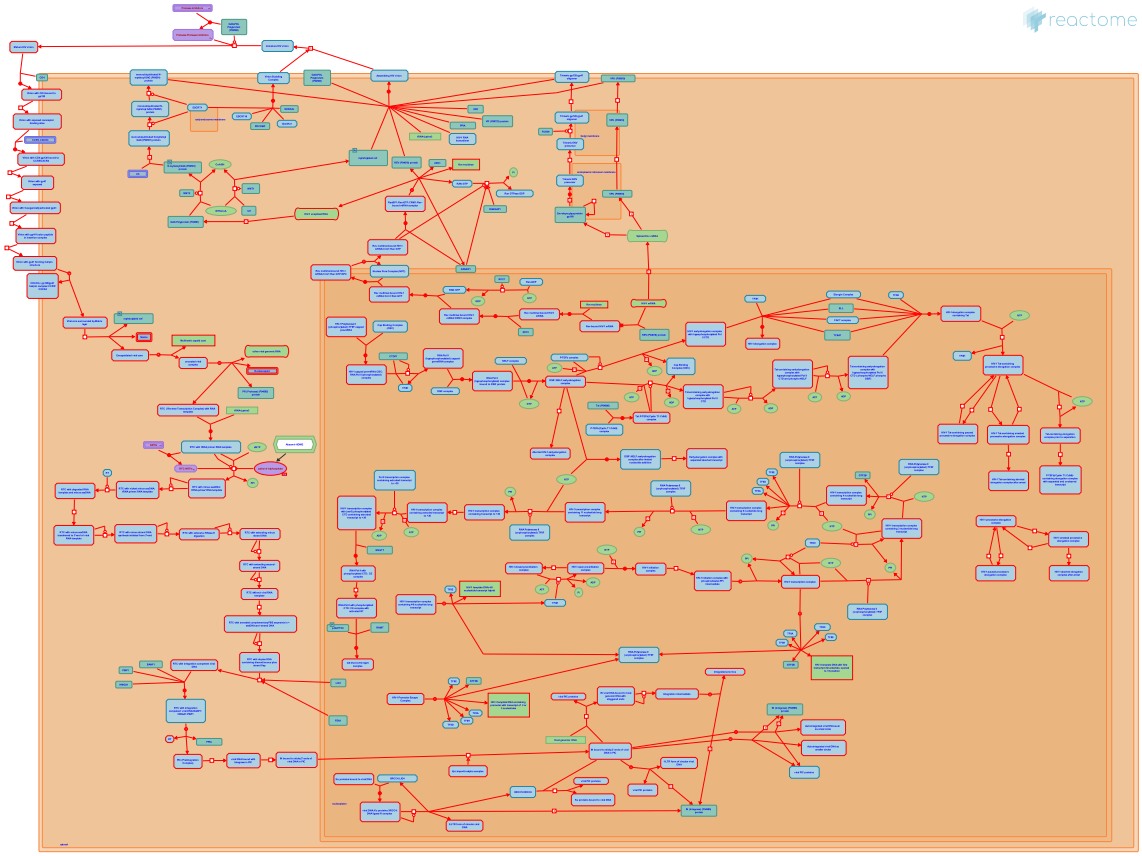
HIV Life Cycle



Aiken, C., Bukrinsky, M., Bushman, FD., D'Eustachio, P., Gillespie, ME., Gopinathrao, G., Hughes, SH., Iordanskiy, S., Matthews, L., Morrow, MP., Peterlin, BM., Reeves, J., Rice, AP.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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.

27/04/2024

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

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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. ↗

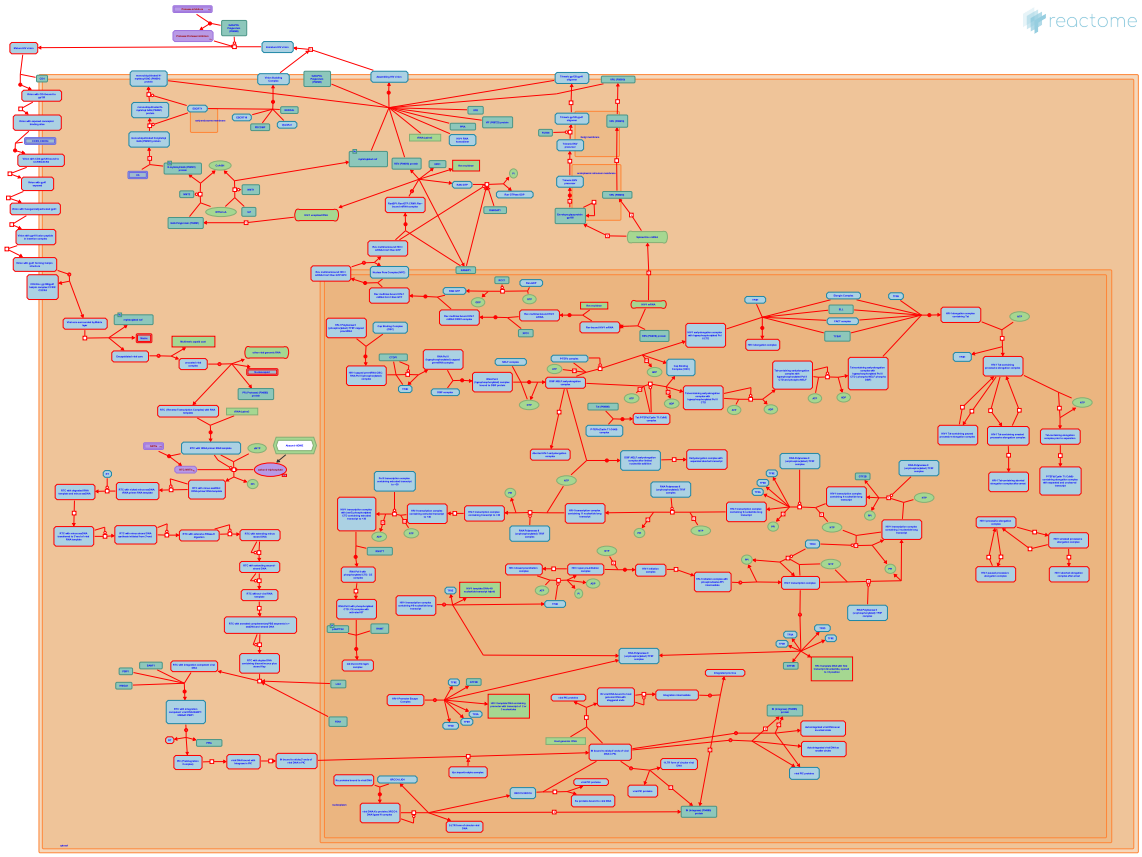
Reactome database release: 88

This document contains 3 pathways (see Table of Contents)

HIV Life Cycle ↗

Stable identifier: R-HSA-162587

Diseases: Human immunodeficiency virus infectious disease



The life cycle of HIV-1 is divided into early and late phases, shown schematically in the figure. In the **early** phase, an HIV-1 virion binds to receptors and co-receptors on the human host cell surface (a), viral and host cell membranes fuse and the viral particle is uncoated (b), the viral genome is reverse transcribed and the viral preintegration complex (PIC) forms (c), the PIC is transported through the nuclear pore into the nucleoplasm (d), and the viral reverse transcript is integrated into a host cell chromosome (e). In the **late** phase, viral RNAs are transcribed from the integrated viral genome and processed to generate viral mRNAs and full-length viral genomic RNAs (f), the viral RNAs are exported through the nuclear pore into the cytosol (g), viral mRNAs are translated and the resulting viral proteins are post-translationally processed (h), core particles containing viral genomic RNA and proteins assemble at the host cell membrane and immature viral particles are released by budding. The released particles mature to become infectious (j), completing the cycle (Frankel and Young 1998; Miller and Bushman 1997).
Most of the crucial concepts used to describe these processes were originally elucidated in studies of retroviruses associated with tumors in chickens, birds, and other animal model systems, and the rapid elucidation of the basic features of the HIV-1 life cycle was critically dependent on the intellectual framework provided by these earlier studies. This earlier work has been very well summarized (e.g., Weiss et al. 1984; Coffin et al. 1997); here for brevity and clarity we focus on experimental studies specific to the HIV-1 life cycle.

Literature references

Varmus, HE., Hughes, SH., Coffin, JM. (1997). Retroviruses. *Cold Spring Harbor Laboratory Press*, 1-843.

Miller, MD., Bushman, FD. (1997). Human immunodeficiency virus type 1 preintegration complexes: studies of organization and composition. *J Virol, 71*, 5382-90. ↗

Frankel, AD., Young, JA. (1998). HIV-1: fifteen proteins and an RNA. *Annu Rev Biochem, 67*, 1-25. ↗

Editions

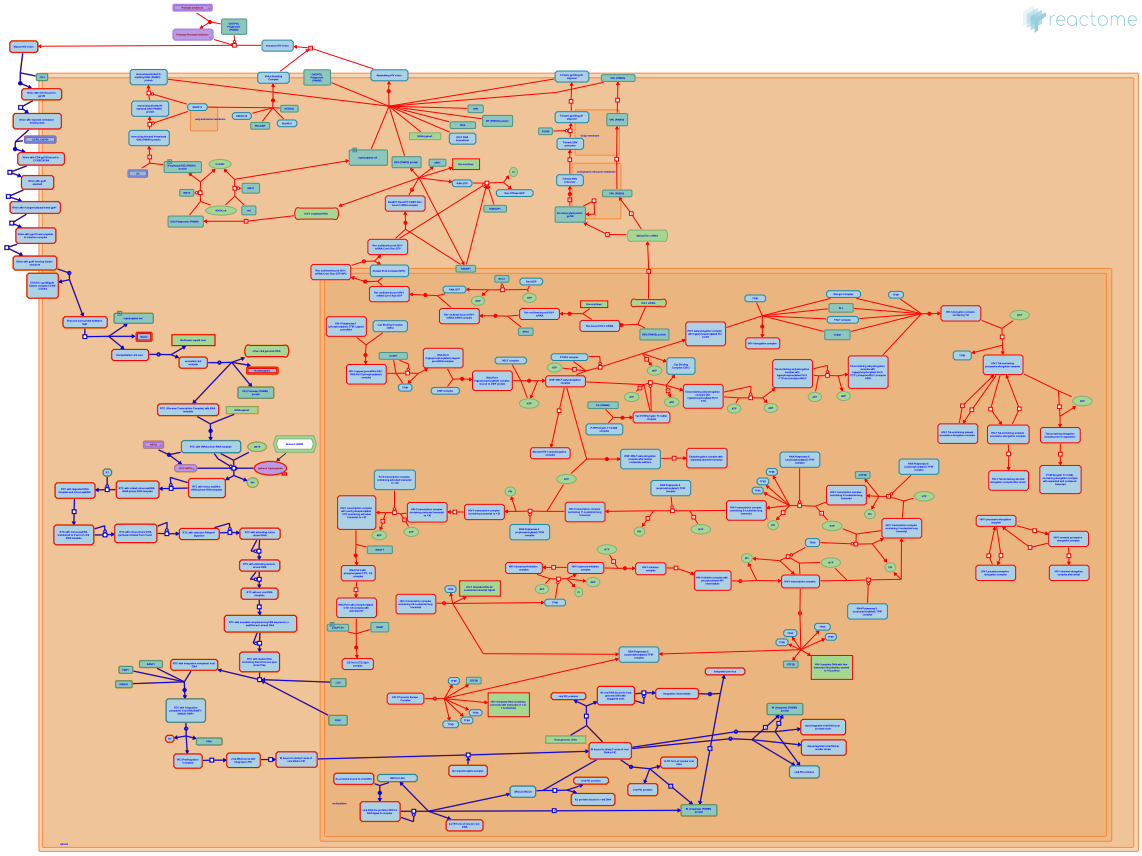
2015-01-13	Authored	Gillespie, ME., Gopinathrao, G., D'Eustachio, P., Matthews, L., Rice, AP., Morrow, MP. et al.

Early Phase of HIV Life Cycle ↗

Location: HIV Life Cycle

Stable identifier: R-HSA-162594

Diseases: Human immunodeficiency virus infectious disease



In the **early phase** of HIV lifecycle, an active virion binds and enters a target cell mainly by specific interactions of the viral envelope proteins with host cell surface receptors. The virion core is uncoated to expose a viral nucleoprotein complex containing RNA and viral proteins. HIV RNA genome is reverse transcribed by the viral Reverse Transcriptase to form a cDNA copy, that gets inserted into host cell DNA. The viral Integrase enzyme is vital to carry out the integration of the viral cDNA into the host genome. The host DNA repair enzymes probably repair the breaks in DNA at the sites of integration.

Literature references

Peterlin, BM., Greene, WC. (2002). Charting HIV's remarkable voyage through the cell: Basic science as a passport to future therapy. *Nat Med, 8*, 673-80. ↗

Editions

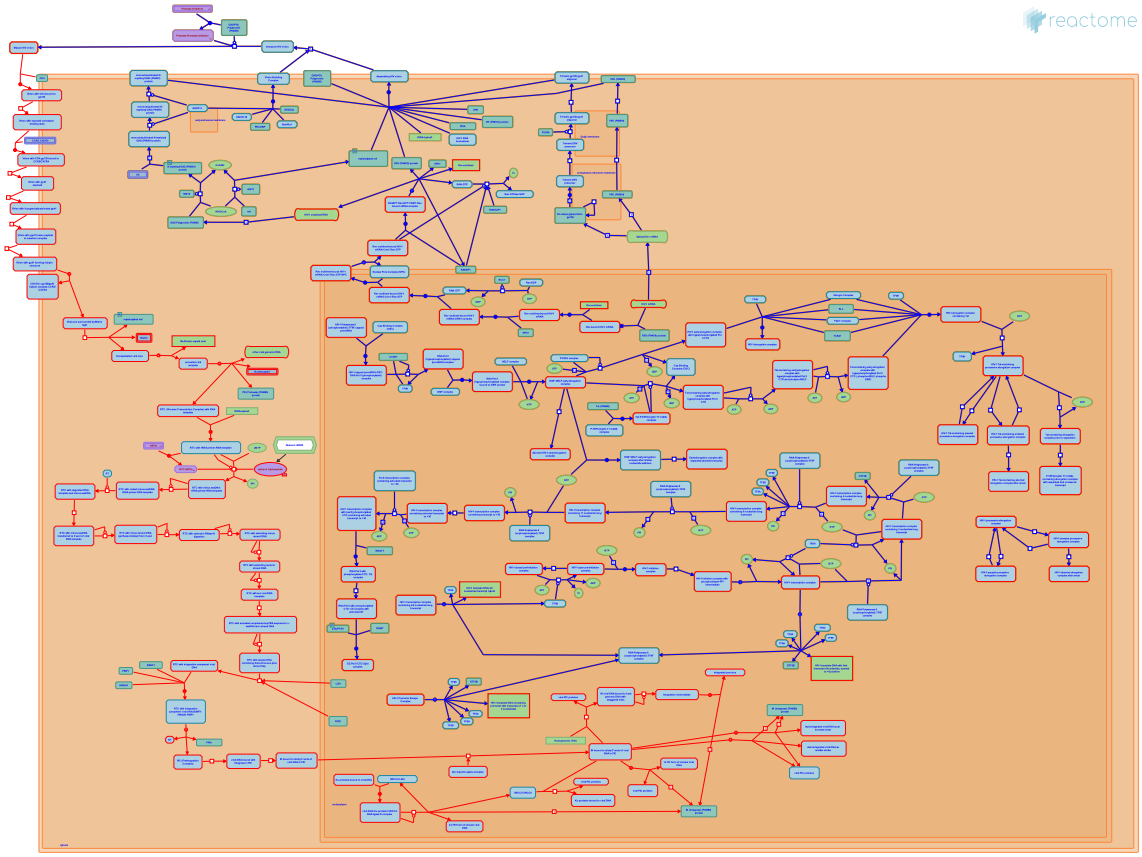
2006-02-17	Edited	Gopinathrao, G.
2006-05-16	Authored	Gopinathrao, G., D'Eustachio, P., Morrow, MP., Iordanskiy, S., Bukrinsky, M.
2006-05-19	Edited	Gopinathrao, G., D'Eustachio, P.
2006-10-31	Reviewed	Aiken, C., Bushman, FD., Hughes, SH., Reeves, J.

Late Phase of HIV Life Cycle ↗

Location: HIV Life Cycle

Stable identifier: R-HSA-162599

Diseases: Human immunodeficiency virus infectious disease



The late phase of the HIV-1 life cycle includes the regulated expression of the HIV gene products and the assembly of viral particles. The assembly of viral particles will be covered in a later release of Reactome. HIV-1 gene expression is regulated by both cellular and viral proteins. Although the initial activation of the HIV-1 transcription is facilitated by cellular transcription factors including NF-kappa B (Nabel and Baltimore, 1987), this activation results in the production of primarily short transcripts (Kao et al., 1987). Expression of high levels of the full length HIV-1 transcript requires the function of the HIV-1 Tat protein which promotes elongation of the HIV-1 transcript (reviewed in Karn, 1999; Taube et al. 1999; Liou et al., 2004; Barboric and Peterlin 2005). The HIV-1 Rev protein is required post-transcriptionally for the expression of the late genes. Rev functions by promoting the nuclear export of unspliced and partially spliced transcripts that encode the major structural proteins Gag, Pol and Env, and the majority of the accessory proteins (Malim et al., 1989; reviewed in Pollard and Malim 1998 .

Literature references

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Peterlin, BM., Barboric, M., Wimmer, J., Taube, R., Fujinaga, K. (1999). Tat transactivation: a model for the regulation of eukaryotic transcriptional elongation. *Virology, 264*, 245-53. ↗

Editions

2005-01-05	Reviewed	Peterlin, BM.
2013-05-23	Revised	Gillespie, ME.

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