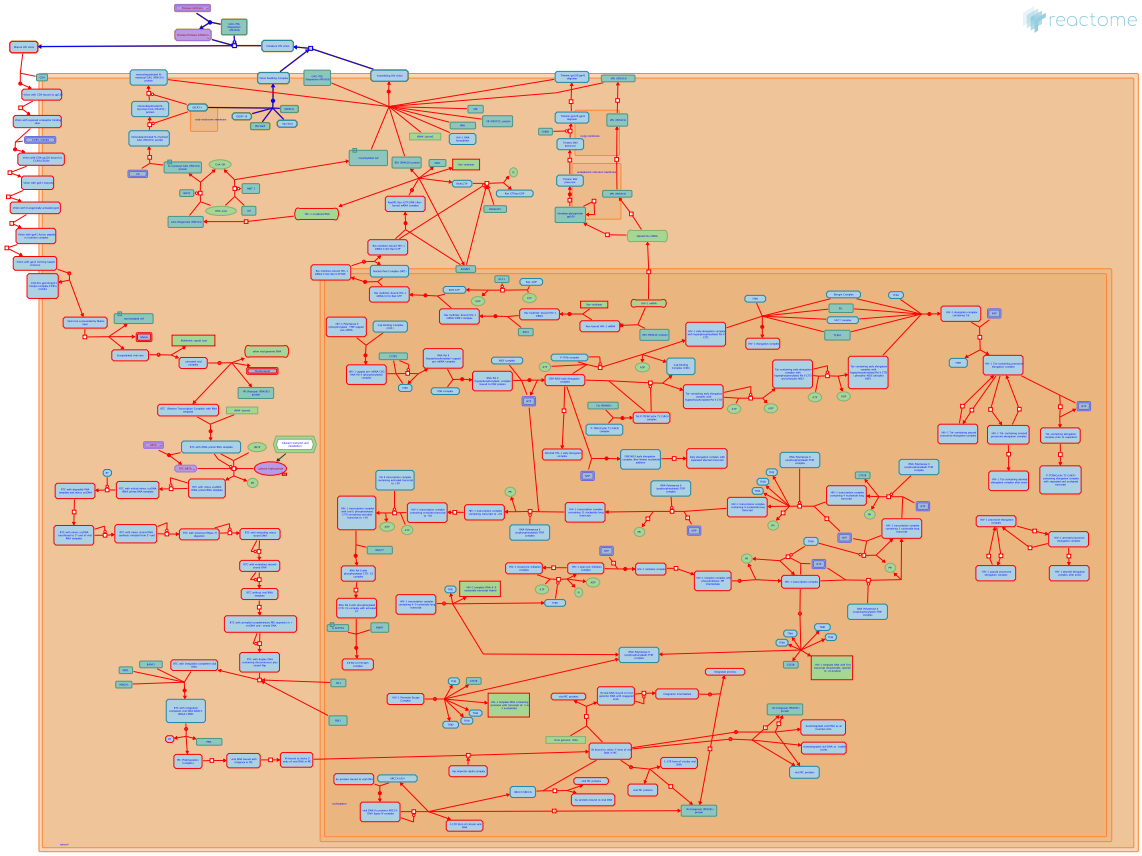
Budding and maturation of HIV virion



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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.

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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. ↗

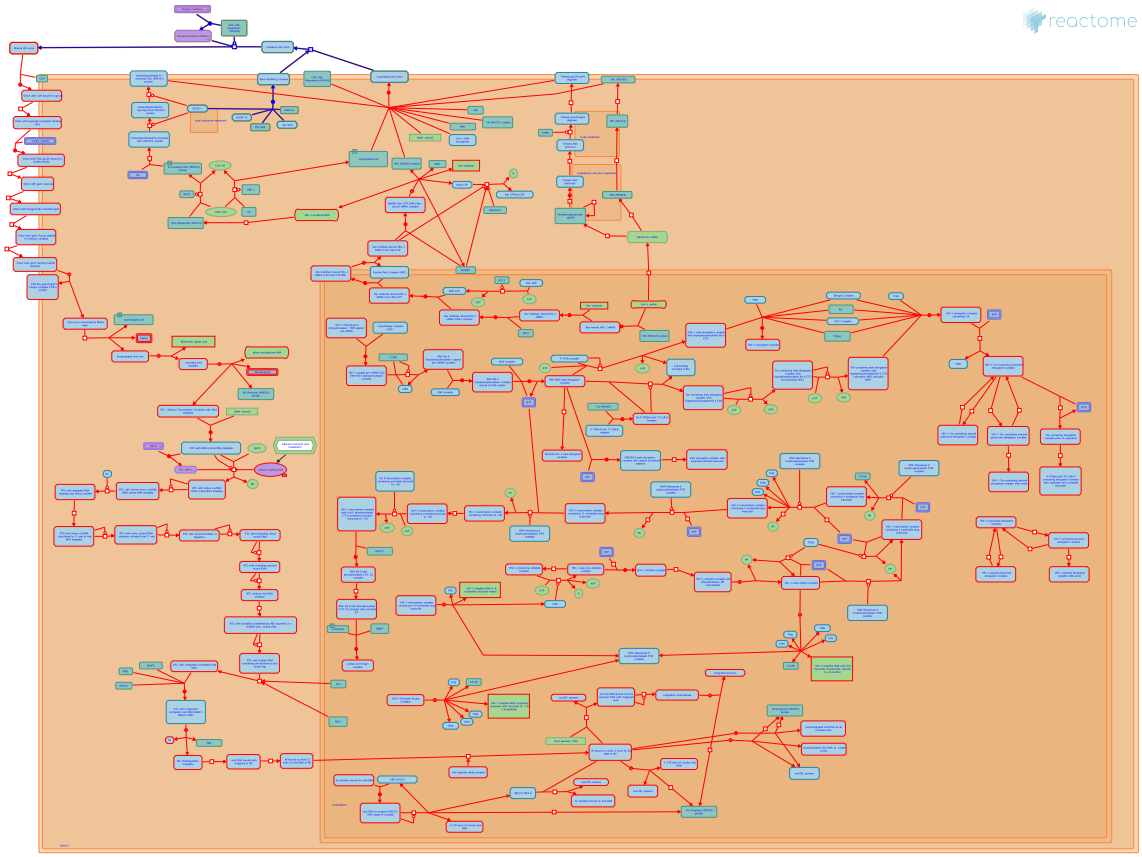
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Budding and maturation of HIV virion ↗

Stable identifier: R-HSA-162588

Diseases: Human immunodeficiency virus infectious disease



With the virus components precariously assembled on the inner leaflet of the plasma membrane, the host cell machinery is required for viral budding. The virus takes advantage of the host ESCRT pathway to terminate Gag polymerization and catalyze release. The ESCRT pathway is normally responsible for membrane fission that creates cytoplasm filled vesicular bodies. In this case HIV (and other viruses) take advantage of the ESCRT cellular machinery to facilitate virion budding from the host.

Literature references

Sundquist, WI., Kräusslich, HG. (2012). HIV-1 Assembly, Budding, and Maturation. *Cold Spring Harb Perspect Med, 2,* a006924. ↗

Editions

2013-03-07	Authored	Gillespie, ME.
2013-05-21	Reviewed	Dube, M.
2013-05-23	Edited	Gillespie, ME.

Recruitment Of HIV Virion Budding Machinery ↗

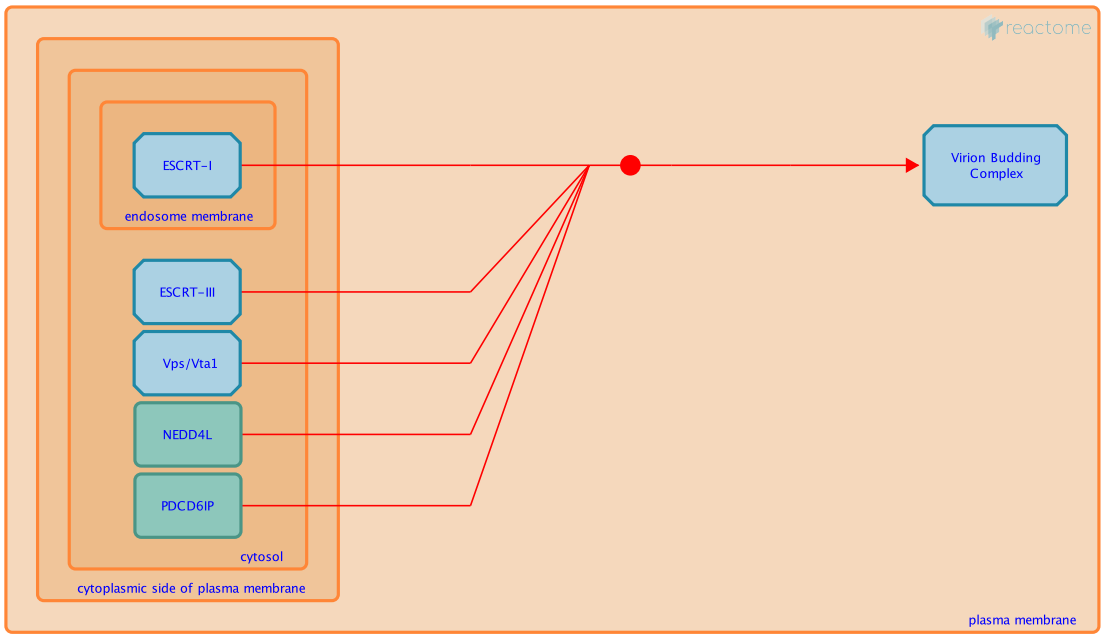
Location: Budding and maturation of HIV virion

Stable identifier: R-HSA-3159232

Type: binding

Compartments: plasma membrane, cytosol, endosome membrane

Diseases: Human immunodeficiency virus infectious disease



The human ESCRT pathway comprises more than 30 different proteins, and this complexity is expanded further by associated regulatory and ubiquitylation machinery. Functional studies have identified a minimal core set of human ESCRT proteins, machinery that is essential for HIV-1 budding. ESCRT-1 recruitment follows an unusal path. The PTAP motif in p6 mimics the ESCRT-1 recruitment motif, bypassing the need for ESCRT-0. The TSG101/ ESCRT-I and ALIX both function by recruiting downstream ESCRT-III and VPS4 complexes, which in turn mediate membrane fission and ESCRT factor recycling.

Followed by: HIV Virion Budding

Literature references

Morita, E., Sundquist, WI. (2004). Retrovirus budding. *Annu Rev Cell Dev Biol, 20*, 395-425. ↗

Sundquist, WI., Kräusslich, HG. (2012). HIV-1 Assembly, Budding, and Maturation. *Cold Spring Harb Perspect Med, 2*, a006924. ↗

Meng, B., Lever, AM. (2013). Wrapping up the bad news: HIV assembly and release. *Retrovirology, 10*, 5. ↗

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2013-05-21	Reviewed	Dube, M.
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HIV Virion Budding ↗

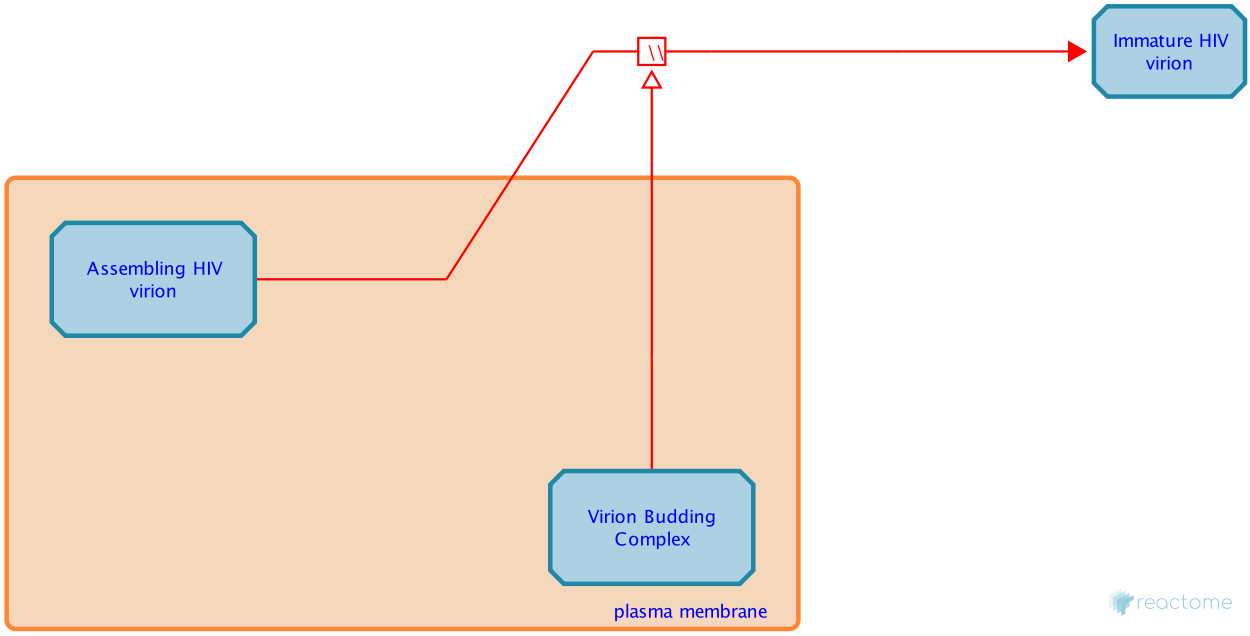
Location: Budding and maturation of HIV virion

Stable identifier: R-HSA-3159227

Type: omitted

Compartments: extracellular region, plasma membrane

Diseases: Human immunodeficiency virus infectious disease



The events that lead to the viral component assembly and the recruitment of the ESCRT host machinery are well-characterized. The exact steps that release the immature viral particle are not. Membrane fission is an energy intensive process and an active area of study.

Preceded by: Recruitment Of HIV Virion Budding Machinery

Followed by: Maturation of HIV Virion

Literature references

Sundquist, WI., Kräusslich, HG. (2012). HIV-1 Assembly, Budding, and Maturation. *Cold Spring Harb Perspect Med, 2*, a006924. ↗

Bieniasz, PD. (2009). The cell biology of HIV-1 virion genesis. *Cell Host Microbe, 5*, 550-8. ↗

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2013-03-07	Authored	Gillespie, ME.
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2013-05-23	Edited	Gillespie, ME.

Maturation of HIV Virion ↗

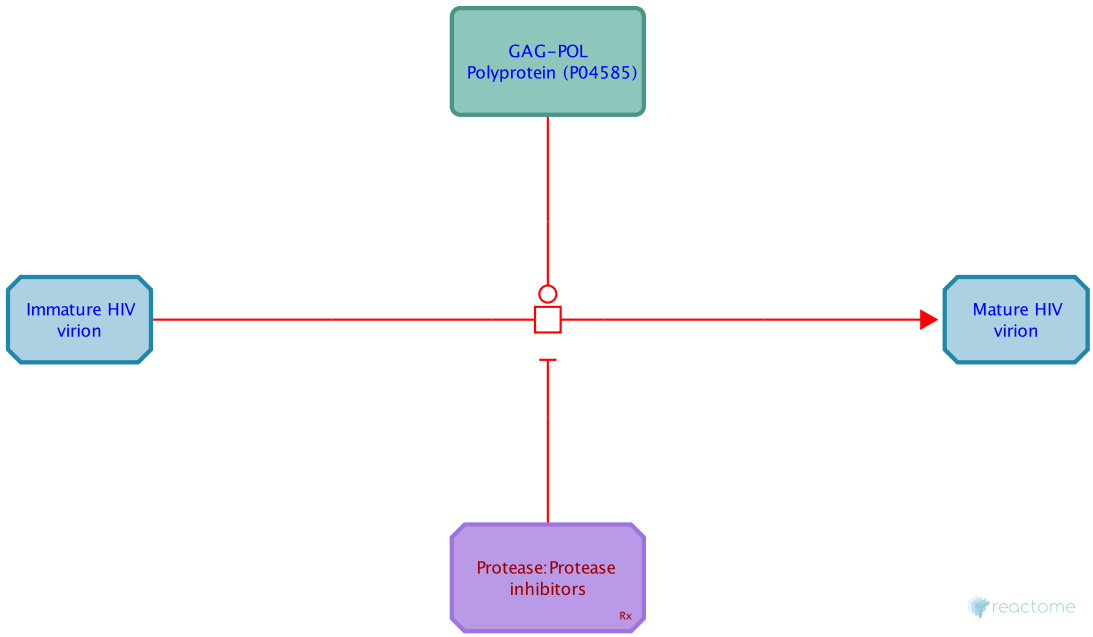
Location: Budding and maturation of HIV virion

Stable identifier: R-HSA-3139027

Type: transition

Compartments: extracellular region

Diseases: Human immunodeficiency virus infectious disease



The proteolytic events that cleave Gag and Gag-Pro-Pol are well characterized, but the event that triggers the protease is not well characterized. The PRGag, that is assembled in the immature virion weakly dimerizes, once PR is cleaved from the proprotein PR dimerizes and becomes an efficient protease. This assembly step may be part of the switch. Once the protease becomes active in the immature virion MA, CA, SP1, NC, SP2, P6, PR, RT, and IN are produced. This event, the production of these fragments would be the switch from immature to mature.

Preceded by: HIV Virion Budding

Literature references

Sundquist, WI., Kräusslich, HG. (2012). HIV-1 Assembly, Budding, and Maturation. *Cold Spring Harb Perspect Med, 2*, a006924. ↗

Bell, NM., Lever, AM. (2013). HIV Gag polyprotein: processing and early viral particle assembly. *Trends Microbiol., 21* , 136-44. ↗

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2013-03-07	Authored	Gillespie, ME.
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Protease binds protease inhibitors ↗

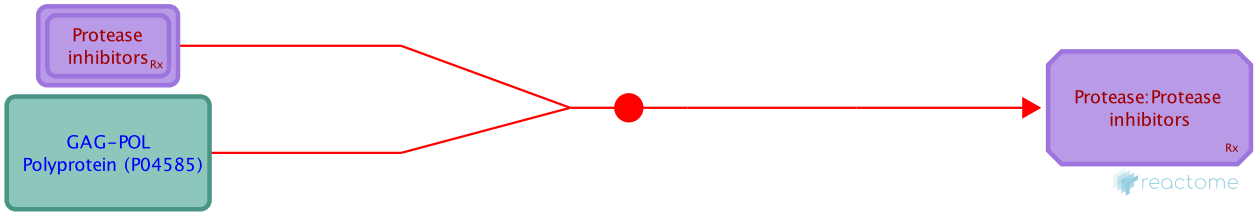
Location: Budding and maturation of HIV virion

Stable identifier: R-HSA-9697043

Type: binding

Compartments: extracellular region

Diseases: Human immunodeficiency virus infectious disease



Antiretroviral (ARV) therapy, comprising a backbone of two nucleos(t)ide reverse transcriptase inhibitors (NRTIs) plus another ARV, has helped extend life expectancy in people living with HIV (Orkin et al. 2018).

Lopinavir is an antiretroviral protease inhibitor used in combination with other antiretrovirals in the treatment of HIV-1 infection. Like many other protease inhibitors, lopinavir is a peptidomimetic molecule; it contains a hydroxyethylene scaffold that mimics the peptide linkage typically targeted by the HIV-1 protease enzyme but which itself cannot be cleaved, thus preventing the acivity of the HIV-1 protease (Reddy et al. 2007). Another HIV protease inhibitor, darunavir, prevents HIV replication through binding to the enzyme, stopping the dimerization and the catalytic activity of HIV-1 protease (De Meyer et al. 2005). In particular, it inhibits the cleavage of HIV encoded Gag-Pol proteins in cells that have been infected with the virus, halting the formation of mature virus particles, which spread the infection (Davis et al. 2012).

Lopinavir in combination with other drugs is currently being investigated for patients with COVID-19 (many clinical trials, example registration nos. ChiCTR2000029603, ChiCTR2000029539, NCT04255017, NCT04261270) (Harrison 2020, Cao et al. 2020, Deng et al. 2020, Martinez 2020).

Literature references

Cao, B., Wang, Y., Wen, D., Liu, W., Wang, J., Fan, G. et al. (2020). A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. *N. Engl. J. Med.*. ↗

Deng, L., Li, C., Zeng, Q., Liu, X., Li, X., Zhang, H. et al. (2020). Arbidol combined with LPV/r versus LPV/r alone against Corona Virus Disease 2019: A retrospective cohort study. *J. Infect.*. ↗

Martinez, MA. (2020). Compounds with therapeutic potential against novel respiratory 2019 coronavirus. *Antimicrob. Agents Chemother.*. ↗

Harrison, C. (2020). Coronavirus puts drug repurposing on the fast track. *Nat. Biotechnol.*. ↗

De Meyer, S., Azijn, H., Surleraux, D., Jochmans, D., Tahri, A., Pauwels, R. et al. (2005). TMC114, a novel human immunodeficiency virus type 1 protease inhibitor active against protease inhibitor-resistant viruses, including a broad range of clinical isolates. *Antimicrob. Agents Chemother., 49*, 2314-21. ↗

Editions

2020-04-21	Authored, Edited	Jassal, B.
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Table of Contents