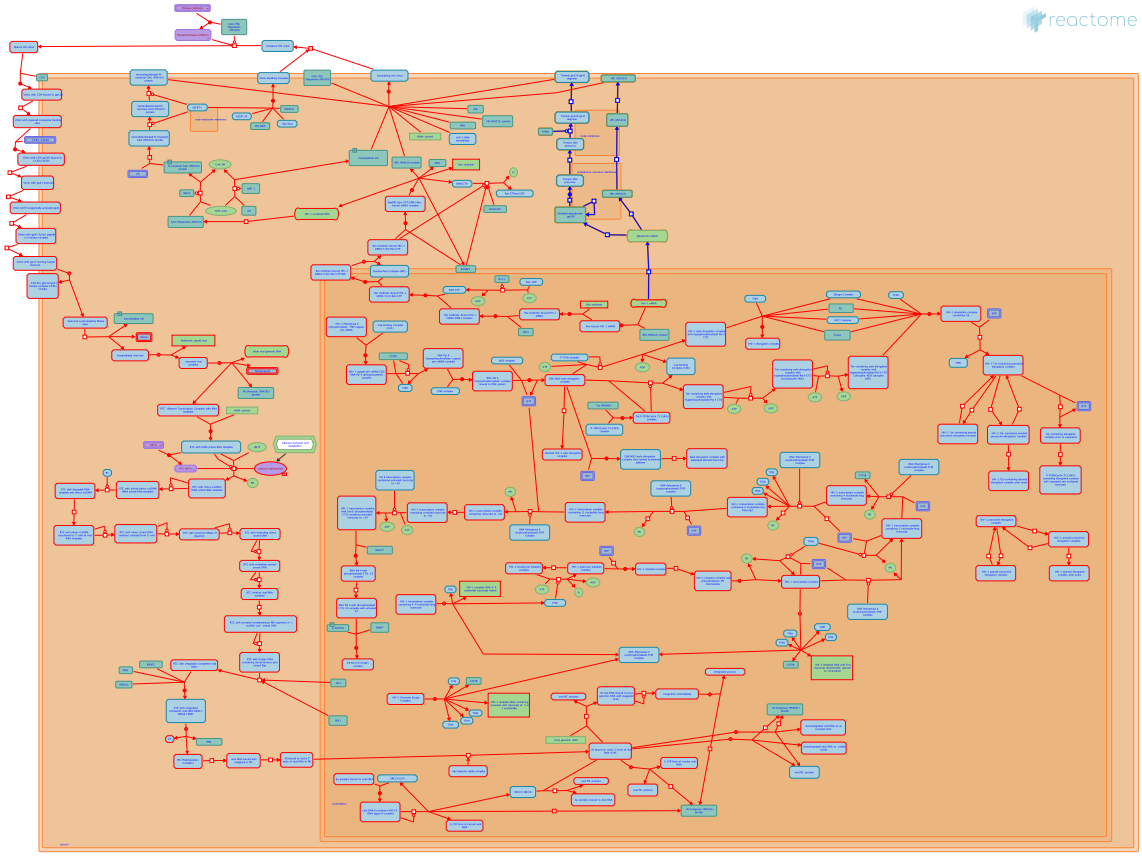
Synthesis and processing of ENV and VPU



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05/09/2021

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. ↗

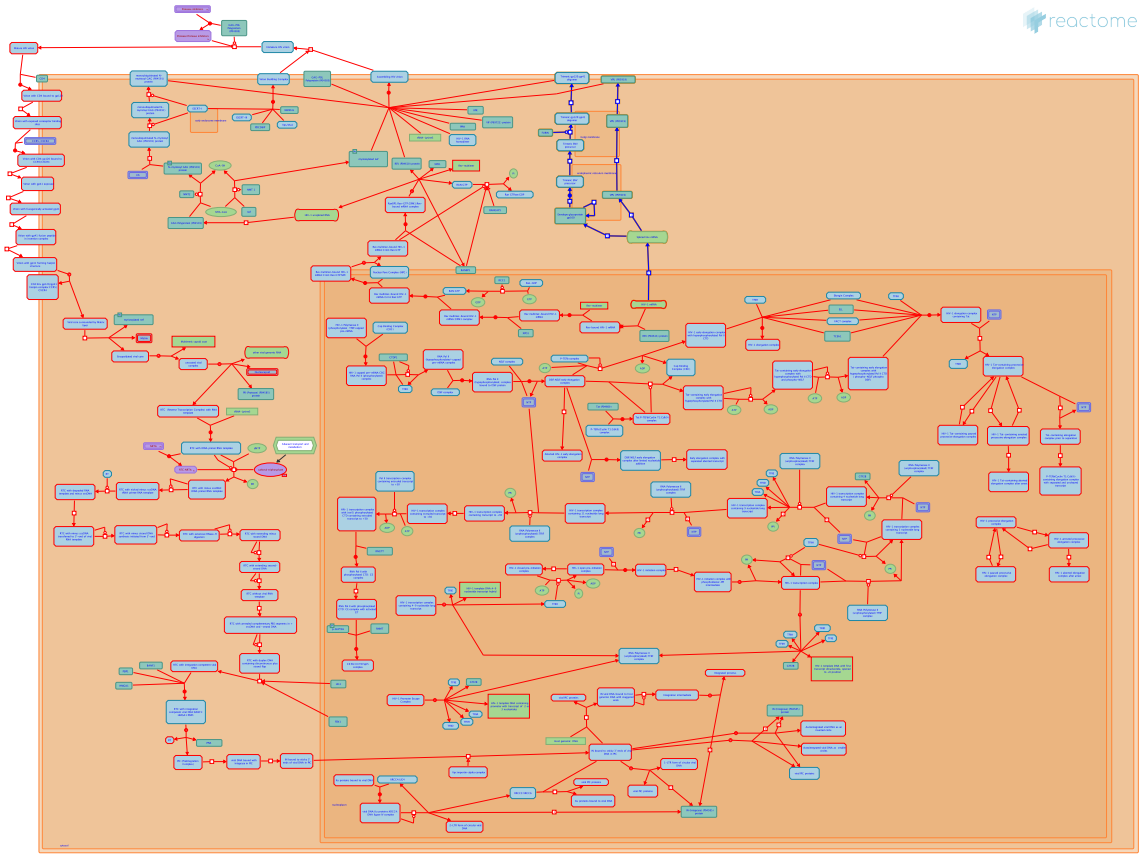
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Synthesis and processing of ENV and VPU ↗

Stable identifier: R-HSA-171286

Diseases: Human immunodeficiency virus infectious disease



The two viral membrane proteins, Env and the accessory protein Vpu, which are encoded by the same mRNA, are translated on the rough ER. All virion components need to traffic from their point of synthesis to sites of assembly on the plasma membrane. Env is an integral membrane protein. It is inserted co-translationally into ER membranes and then travels through the cellular secretory pathway where it is glycosylated, assembled into trimeric complexes, processed into the gp41 and gp120 subunits by the cellular protease furin.

Literature references

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

Editions

2013-01-30	Edited	Gillespie, ME.
2013-03-07	Authored	Gillespie, ME.
2013-05-21	Reviewed	Dube, M.

Splicing of HIV RNA transcript ↗

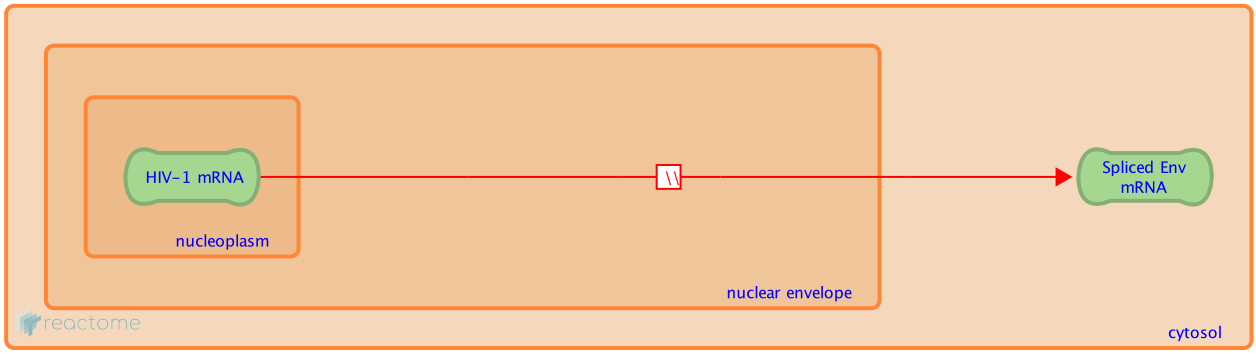
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-187211

Type: omitted

Compartments: nuclear envelope

Diseases: Human immunodeficiency virus infectious disease



HIV is characterized by the production of multiple-spliced RNA species. The genomic fragmant is processesed creating multiple mRNA fragments.

Followed by: Synthesis of ENV polyprotein, Synthesis of VPU protein

Literature references

Tazi, J., Bakkour, N., Marchand, V., Ayadi, L., Aboufirassi, A., Branlant, C. (2010). Alternative splicing: regulation of HIV-1 multiplication as a target for therapeutic action. *FEBS J., 277*, 867-76. ↗

Editions

2013-01-30	Edited	Gillespie, ME.
2013-03-07	Authored	Gillespie, ME.
2013-05-21	Reviewed	Dube, M.

Synthesis of ENV polyprotein ↗

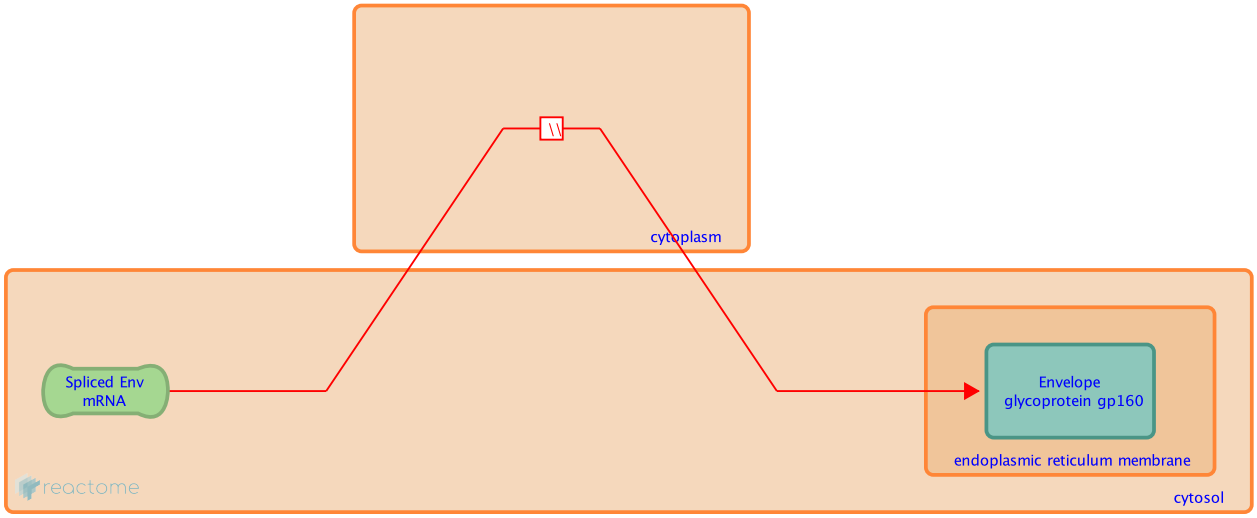
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-174494

Type: omitted

Compartments: cytoplasm

Diseases: Human immunodeficiency virus infectious disease



The ENV precursor protein gp160 is synthesized.

Preceded by: Splicing of HIV RNA transcript

Followed by: Glycosylation of ENV polyprotein

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.

Glycosylation of ENV polyprotein ↗

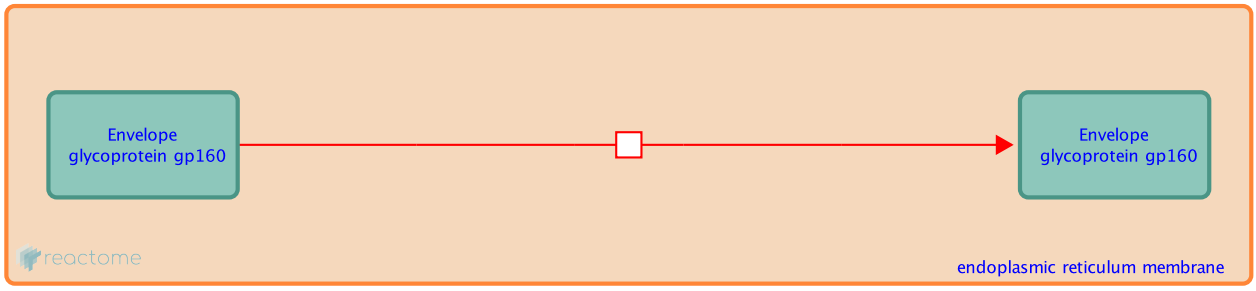
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-174493

Type: transition

Compartments: endoplasmic reticulum membrane

Diseases: Human immunodeficiency virus infectious disease



There are numerous N-linked glycosylation sites that are important for infectivity of human immunodeficiency virus type 1. With more than 20 consensus N-linked glycosylation sites in gp120 it is expected that a number are important for virion function.

Preceded by: Synthesis of ENV polyprotein

Followed by: Folding and Oligomerization of ENV glycoprotein

Literature references

Lee, WR., Syu, WJ., Du, B., Matsuda, M., Tan, S., Wolf, A. et al. (1992). Nonrandom distribution of gp120 N-linked glycosylation sites important for infectivity of human immunodeficiency virus type 1. *Proc. Natl. Acad. Sci. U.S.A.*, *89*, 2213-7. ↗

Editions

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

Folding and Oligomerization of ENV glycoprotein ↗

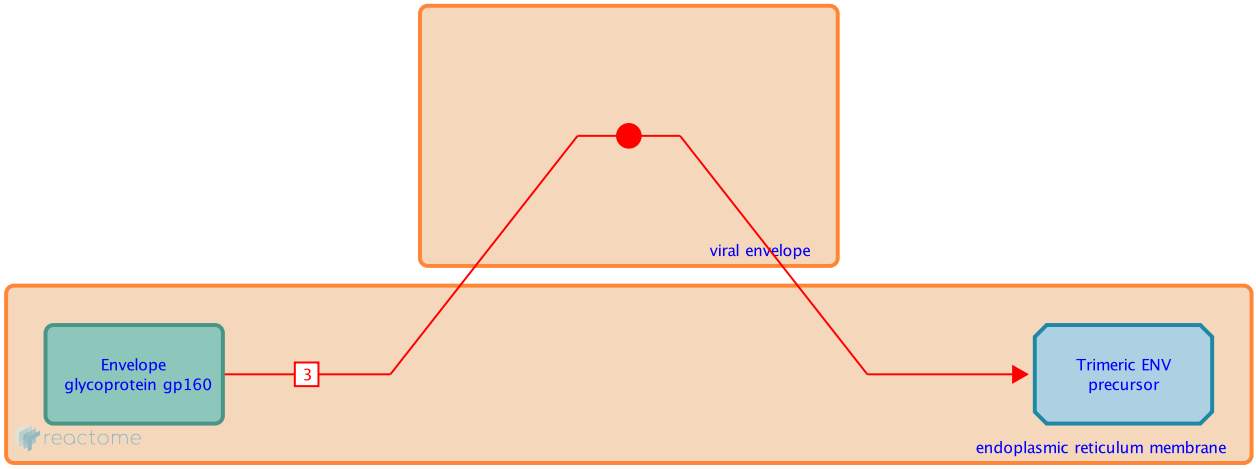
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-171291

Type: binding

Compartments: viral envelope

Diseases: Human immunodeficiency virus infectious disease



The monomeric GP160 ENV precursor protein assembles into a trimer.

Preceded by: Glycosylation of ENV polyprotein

Followed by: Transport of trimeric ENV precursor to Golgi apparatus

Literature references

Zhu, P., Liu, J., Bess, J., Chertova, E., Lifson, JD., Grisé, H. et al. (2006). Distribution and three-dimensional structure of AIDS virus envelope spikes. *Nature, 441*, 847-52. ↗

Editions

2006-04-02	Authored	Gopinathrao, G.
2013-05-21	Reviewed	Dube, M.
2013-05-23	Edited	Gillespie, ME.

Transport of trimeric ENV precursor to Golgi apparatus ↗

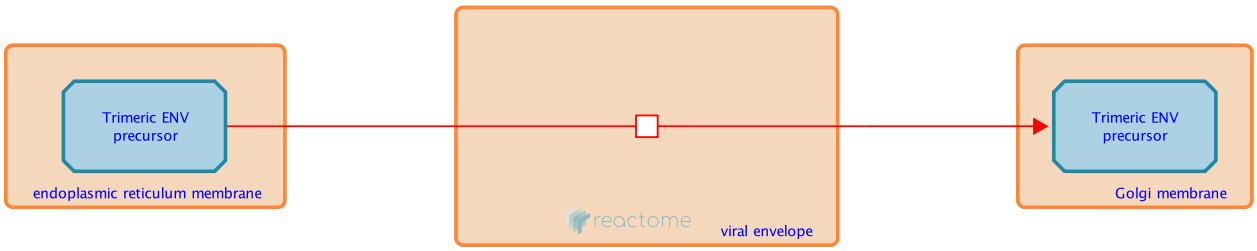
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-174491

Type: transition

Compartments: viral envelope

Diseases: Human immunodeficiency virus infectious disease



The trimeric ENV precursor complex is transported from the ER to the Golgi.

Preceded by: Folding and Oligomerization of ENV glycoprotein

Followed by: Cleavage of the viral Env gp160 precursor polyprotein

Literature references

Welman, M., Lemay, G., Cohen, EA. (2007). Role of envelope processing and gp41 membrane spanning domain in the formation of human immunodeficiency virus type 1 (HIV-1) fusion-competent envelope glycoprotein complex. *Virus Res., 124*, 103-12. ↗

Editions

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

Cleavage of the viral Env gp160 precursor polyprotein ↗

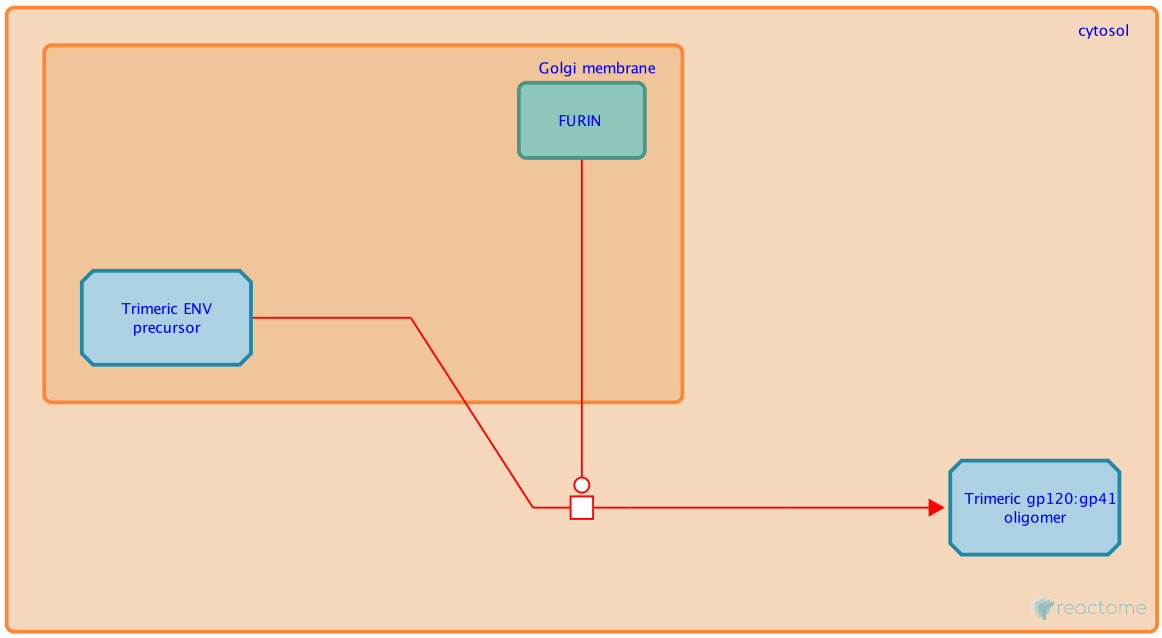
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-171288

Type: transition

Compartments: cytosol

Diseases: Human immunodeficiency virus infectious disease



The trimeric gp160 complexes are cleaved into the gp41 and gp120 subunits by the cellular protease furin.

Preceded by: Transport of trimeric ENV precursor to Golgi apparatus

Followed by: Transport of trimeric gp41:gp120 to plasma membrane

Literature references

Decroly, E., Vandenbranden, M., Ruysschaert, JM., Cogniaux, J., Jacob, GS., Howard, SC. et al. (1994). The convertases furin and PC1 can both cleave the human immunodeficiency virus (HIV)-1 envelope glycoprotein gp160 into gp120 (HIV-1 SU) and gp41 (HIV-I TM). *J. Biol. Chem., 269*, 12240-7. ↗

Editions

2006-02-10	Authored	Gopinathrao, G.
2013-05-21	Reviewed	Dube, M.
2013-05-23	Edited	Gillespie, ME.

Transport of trimeric gp41:gp120 to plasma membrane

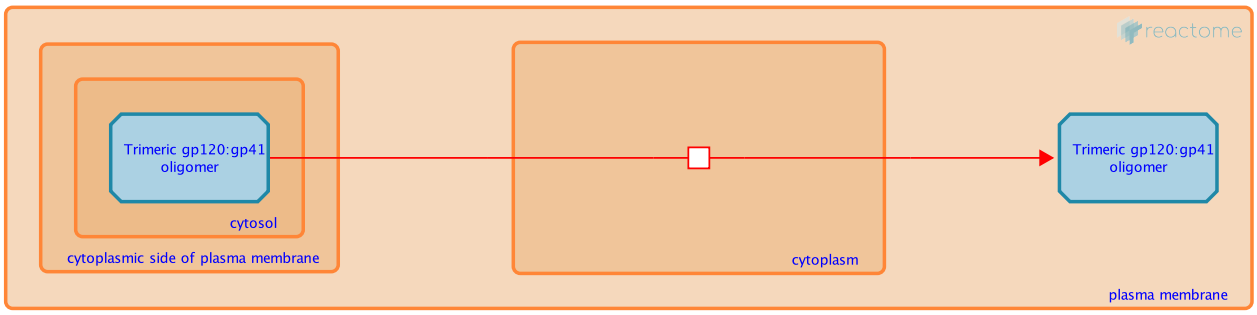
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-173647

Type: transition

Compartments: cytoplasm

Diseases: Human immunodeficiency virus infectious disease



The cleaved and assembled gp41:gp121 complexes are transport to teh plasma membrane. This complex ultimately arrives via the cellular secretion pathway. Env is an integral membrane protein shuttled through the ER and Golgi where it was glycosylated and cleaved into the gp41 and gp120 subunits. The trimeric complex is brought to the plasma membrane by the host vesicular transport system. Only 7-14 trimers are present per virion.

Preceded by: Cleavage of the viral Env gp160 precursor polyprotein

Literature references

Helseth, E., Olshevsky, U., Furman, C., Sodroski, J. (1991). Human immunodeficiency virus type 1 gp120 envelope glycoprotein regions important for association with the gp41 transmembrane glycoprotein. *J Virol, 65*, 2119-23.

Editions

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

Synthesis of VPU protein ↗

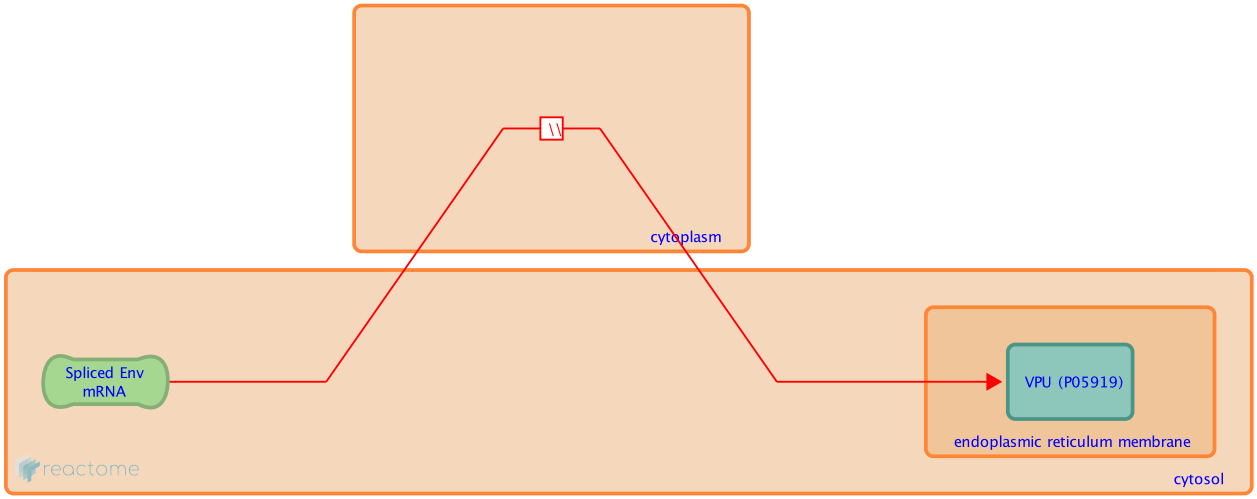
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-3149433

Type: omitted

Compartments: cytoplasm

Diseases: Human immunodeficiency virus infectious disease



As the Rev protein accumulates, nuclear export of the singly and unspliced mRNAs is facilitated. These mRNAs express the Vif, Vpr, Vpu, Env proteins and the Gag and Gag-Pol polyproteins, respectively, and require Rev, which overcomes the restriction of nuclear export of intron-containing transcripts by accessing the CRM1 nuclear export pathway

Preceded by: Splicing of HIV RNA transcript

Followed by: Transport of VPU to Golgi apparatus

Literature references

Tazi, J., Bakkour, N., Marchand, V., Ayadi, L., Aboufirassi, A., Branlant, C. (2010). Alternative splicing: regulation of HIV-1 multiplication as a target for therapeutic action. *FEBS J., 277*, 867-76. ↗

Editions

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

Transport of VPU to Golgi apparatus ↗

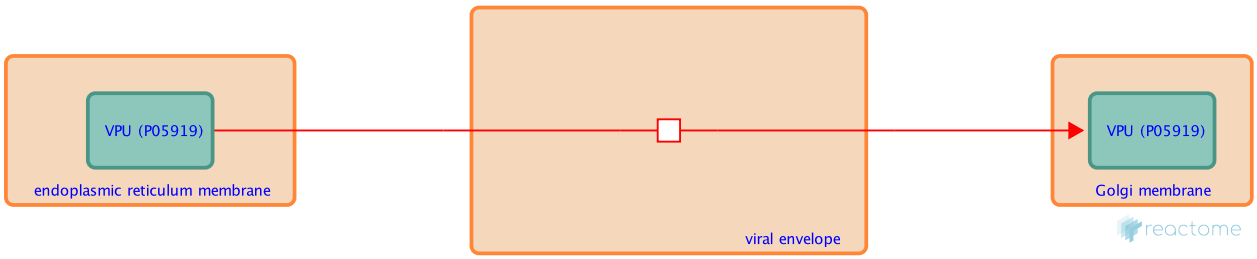
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-3149440

Type: transition

Compartments: viral envelope

Diseases: Human immunodeficiency virus infectious disease



VPU is shuttled through the ER:Golgi protein expression pathway.

Preceded by: Synthesis of VPU protein

Followed by: Transport of VPU to Plasma Membrane

Literature references

Malim, MH., Bieniasz, PD. (2012). HIV Restriction Factors and Mechanisms of Evasion. *Cold Spring Harb Perspect Med , 2*, a006940. ↗

Editions

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

Transport of VPU to Plasma Membrane ↗

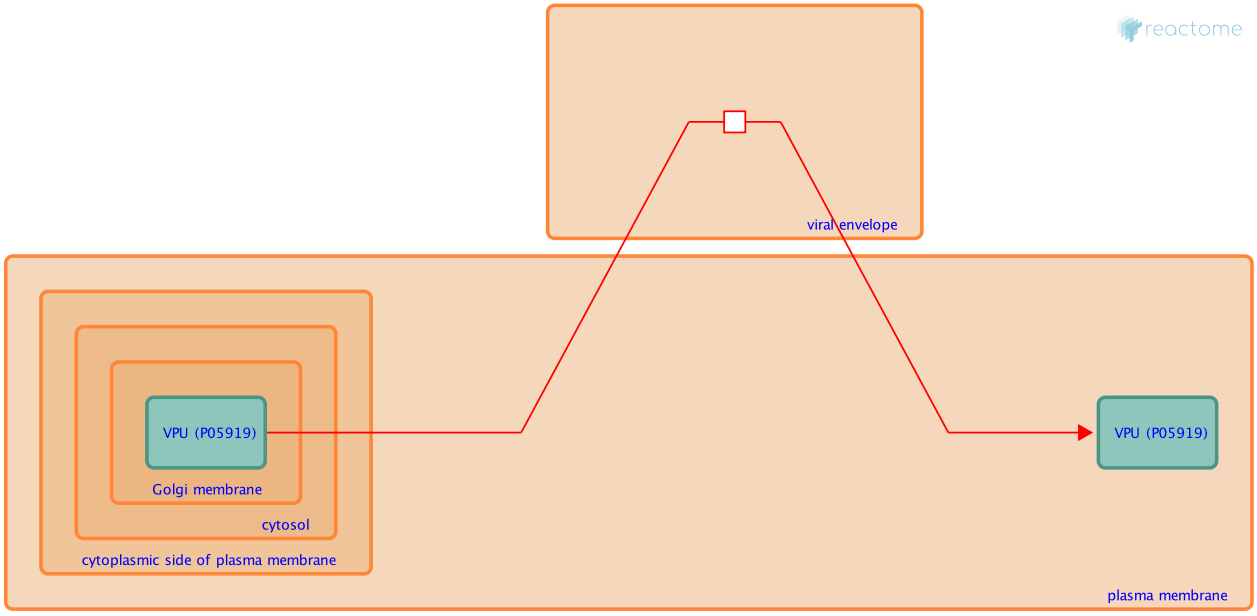
Location: Synthesis and processing of ENV and VPU

Stable identifier: R-HSA-3149432

Type: transition

Compartments: viral envelope

Diseases: Human immunodeficiency virus infectious disease



Once transported to the plasma membrane the VPU protein will be incorporated into the assembling virus. The Vpu accessory protein is found to be required for efficient virion release from some cell lines but completely dispensible in others.

Preceded by: Transport of VPU to Golgi apparatus

Literature references

Malim, MH., Bieniasz, PD. (2012). HIV Restriction Factors and Mechanisms of Evasion. *Cold Spring Harb Perspect Med , 2*, a006940. ↗

Editions

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

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