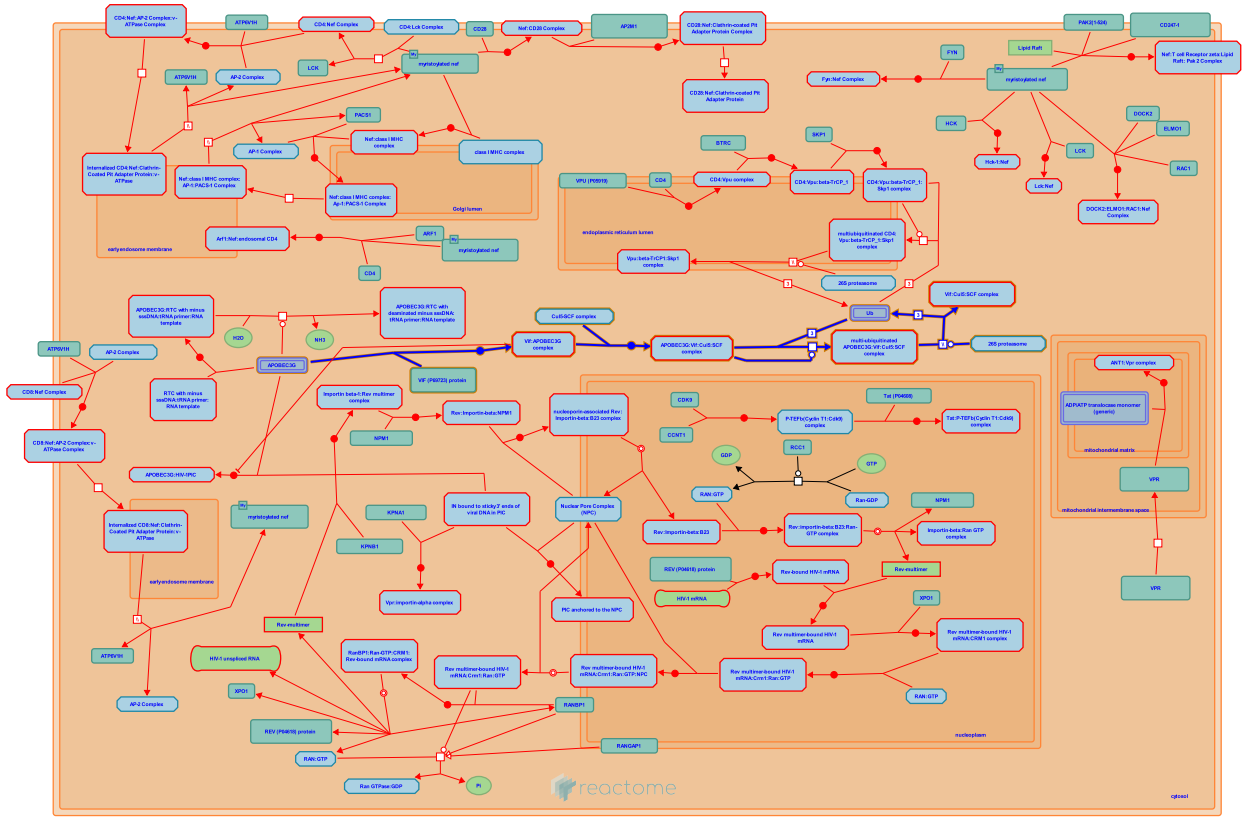
Vif-mediated degradation of APOBEC3G



Matthews, L., Mulder, L., Simon, V.

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

05/05/2024

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

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. ↗

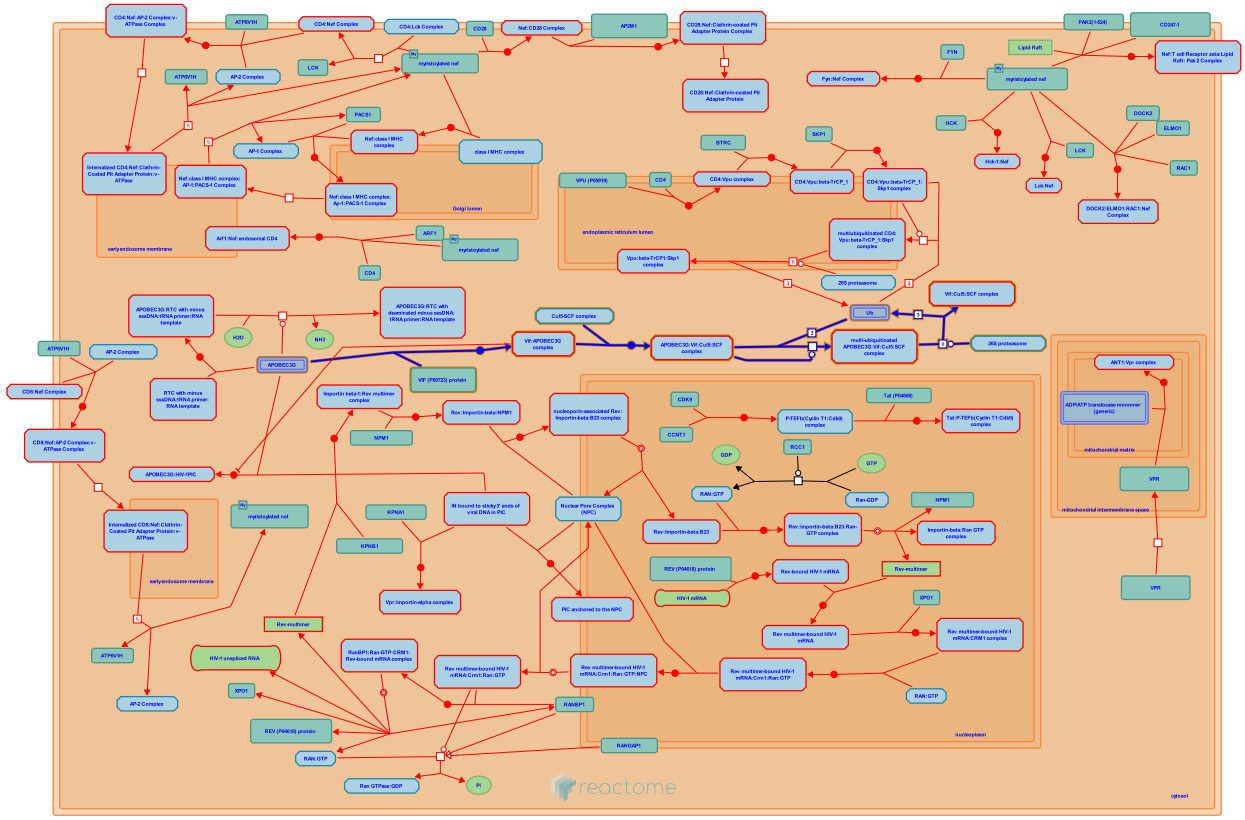
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Vif-mediated degradation of APOBEC3G ↗

Stable identifier: R-HSA-180585

Compartments: cytosol

Diseases: Human immunodeficiency virus infectious disease



The HIV-1 accessory protein Vif (Viral infectivity factor) is required for the efficient infection of primary cell populations (e.g., lymphocytes and macrophages) and 'non-permissive' cell lines. Vif neutralises the host DNA editing enzyme, APOBEC3G, in the producer cell. Indeed, in the absence of a functional Vif, APOBEC3G is selectively incorporated into the budding virions and in the next cycle of infection leads to the deamination of deoxycytidines (dC) within the minus-strand cDNA during reverse transcription (Sheehy et al 2003; Li et al., 2005 ; Stopak et al. 2003).
Deamination changes cytidine to uracil and thus results in G to A transitions and stop codons in the provirus. The aberrant cDNAs produced in the infected cell can either be integrated in form of non-functional proviruses or degraded. Vif counteracts the antiviral activity of APOBEC3G by associating directly with it and promoting its polyubiquitination and degradation by the 26S proteasome.
Vif binds APOBEC3G and recruits it into an E3 ubiquitin-enzyme complex composed by the cytoplasmic proteins Cullin5, Rbx, ElonginC and ElonginB (Yu et al., 2003) . Thus, in the presence of Vif, APOBEC3G incorporation into the virion is minimal.

Literature references

Uchiyama, T., Takaori-Kondo, A., Miyauchi, Y., Iwai, K., Kobayashi, M. (2005). Ubiquitination of APOBEC3G by an HIV-1 Vif-Cullin5-Elongin B-Elongin C complex is essential for Vif function. *J Biol Chem, 280*, 18573-8. ↗

Yu, XF., Luo, K., Kong, W., Mao, P., Liu, B., Yu, X. et al. (2003). Induction of APOBEC3G ubiquitination and degradation by an HIV-1 Vif-Cul5-SCF complex. *Science, 302*, 1056-60. ↗

Gaddis, NC., Sheehy, AM., Malim, MH. (2003). The antiretroviral enzyme APOBEC3G is degraded by the proteasome in response to HIV-1 Vif. *Nat Med, 9*, 1404-7. ↗

Editions

2006-05-16	Authored	Matthews, L.
2007-01-30	Edited	Matthews, L.
2007-01-31	Reviewed	Simon, V., Mulder, L.

Association of Vif with APOBEC3G ↗

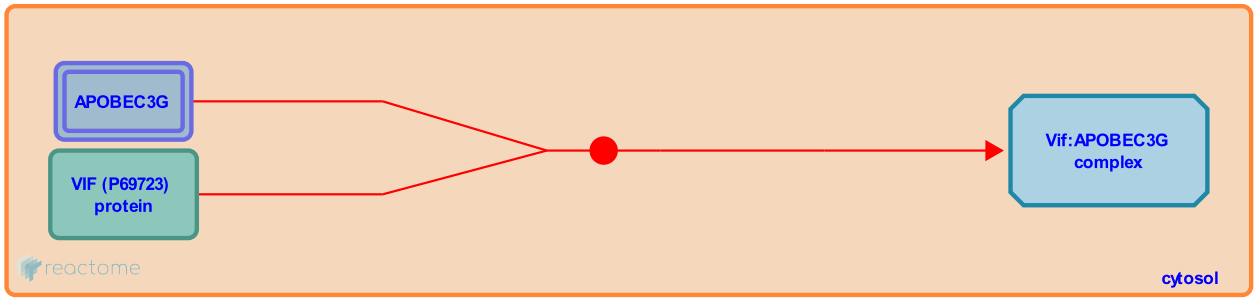
Location: Vif-mediated degradation of APOBEC3G

Stable identifier: R-HSA-180602

Type: binding

Compartments: cytosol

Diseases: Human immunodeficiency virus infectious disease



The HIV-1 Vif protein associates with the DNA editing enzyme APOBEC3G Marin et al) . The binding site has not yet been mapped but emerging evidence suggest that the N-terminal lregion of Vif is essential for APOBEC3G recognition (Tian et al) .
Substitution of a single amino acid in the human APOBEC3G (Asp128Lys) abolishes binding and renders it resistant to HIV-1 Vif (Schrofelbauer et al; Bogerd et al.).

Followed by: Association of APOBEC3G:Vif with the Cul5-SCF complex

Literature references

Kabat, D., Rose, KM., Kozak, SL., Marin, M. (2003). HIV-1 Vif protein binds the editing enzyme APOBEC3G and induces its degradation. *Nat Med, 9*, 1398-403. ↗

Editions

2006-05-16	Authored	Matthews, L.
2007-01-30	Edited	Matthews, L.
2007-01-31	Reviewed	Simon, V., Mulder, L.

Association of APOBEC3G:Vif with the Cul5-SCF complex ↗

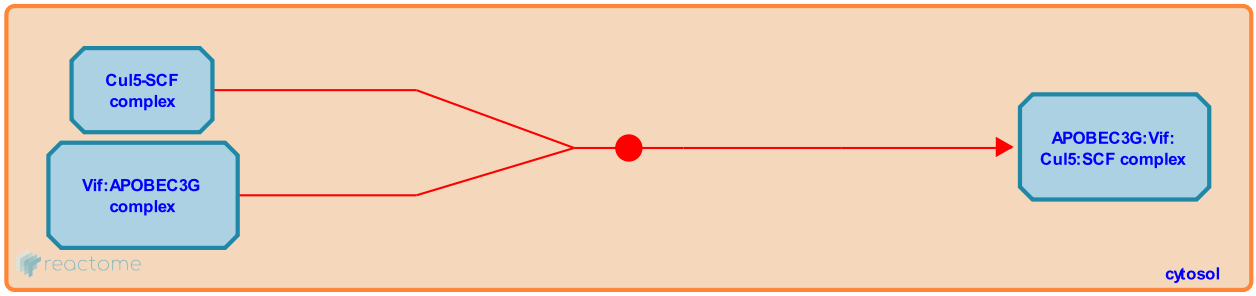
Location: Vif-mediated degradation of APOBEC3G

Stable identifier: R-HSA-180555

Type: binding

Compartments: cytosol

Diseases: Human immunodeficiency virus infectious disease



The interaction between Vif and the E3 ubiquitin ligase complex (Cullin5, Elongin B and Elongin C, and Rbx1) takes place through direct binding of the SOCS box motif in the viral protein Vif to the host protein Elongin C. Moreover, a conserved HCCH motif in Vif allows binding to Cullin 5.

Preceded by: Association of Vif with APOBEC3G

Followed by: Multi-ubiquitination of APOBEC3G

Literature references

Yu, XF., Luo, K., Kong, W., Mao, P., Liu, B., Yu, X. et al. (2003). Induction of APOBEC3G ubiquitination and degradation by an HIV-1 Vif-Cul5-SCF complex. *Science, 302*, 1056-60. ↗

Editions

2006-05-16	Authored	Matthews, L.
2007-01-30	Edited	Matthews, L.
2007-01-31	Reviewed	Simon, V., Mulder, L.

Multi-ubiquitination of APOBEC3G ↗

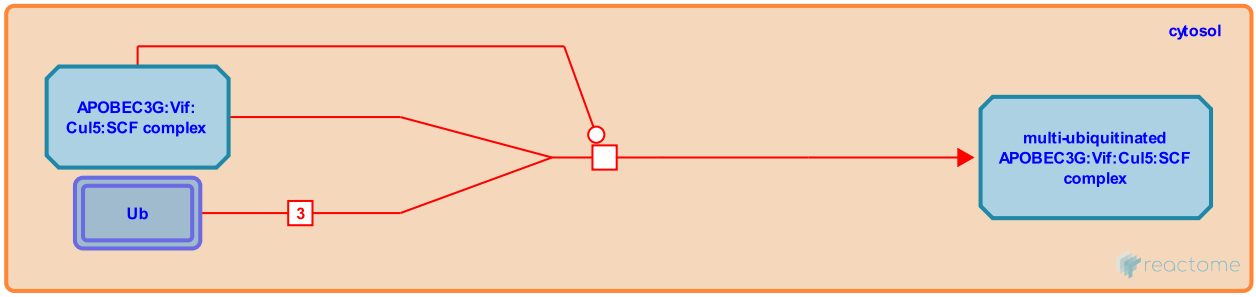
Location: Vif-mediated degradation of APOBEC3G

Stable identifier: R-HSA-180540

Type: transition

Compartments: cytosol

Diseases: Human immunodeficiency virus infectious disease



APOBEC3G is multi-ubiquitinated by the Vif-Cul5-SCF complex.

Preceded by: Association of APOBEC3G:Vif with the Cul5-SCF complex

Followed by: Proteosome-mediated degradation of APOBEC3G

Literature references

Uchiyama, T., Takaori-Kondo, A., Miyauchi, Y., Iwai, K., Kobayashi, M. (2005). Ubiquitination of APOBEC3G by an HIV-1 Vif-Cullin5-Elongin B-Elongin C complex is essential for Vif function. *J Biol Chem, 280*, 18573-8. ↗

Editions

2006-05-16	Authored	Matthews, L.
2007-01-30	Edited	Matthews, L.
2007-01-31	Reviewed	Simon, V., Mulder, L.

Proteosome-mediated degradation of APOBEC3G ↗

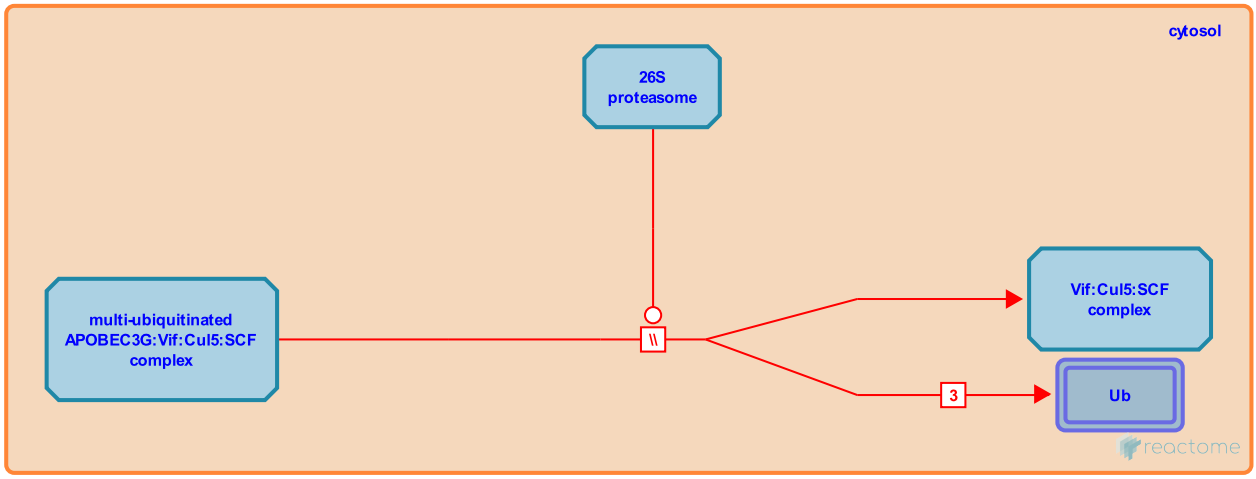
Location: Vif-mediated degradation of APOBEC3G

Stable identifier: R-HSA-180603

Type: omitted

Compartments: cytosol

Diseases: Human immunodeficiency virus infectious disease



Following multi-ubiquitination by the Vif-Cul5-SCF complex, APOBEC3G is degraded by the 26S proteasome.

Preceded by: Multi-ubiquitination of APOBEC3G

Literature references

Uchiyama, T., Takaori-Kondo, A., Miyauchi, Y., Iwai, K., Kobayashi, M. (2005). Ubiquitination of APOBEC3G by an HIV-1 Vif-Cullin5-Elongin B-Elongin C complex is essential for Vif function. *J Biol Chem, 280*, 18573-8. ↗

Yu, XF., Luo, K., Kong, W., Mao, P., Liu, B., Yu, X. et al. (2003). Induction of APOBEC3G ubiquitination and degradation by an HIV-1 Vif-Cul5-SCF complex. *Science, 302*, 1056-60. ↗

Gaddis, NC., Sheehy, AM., Malim, MH. (2003). The antiretroviral enzyme APOBEC3G is degraded by the proteasome in response to HIV-1 Vif. *Nat Med, 9*, 1404-7. ↗

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