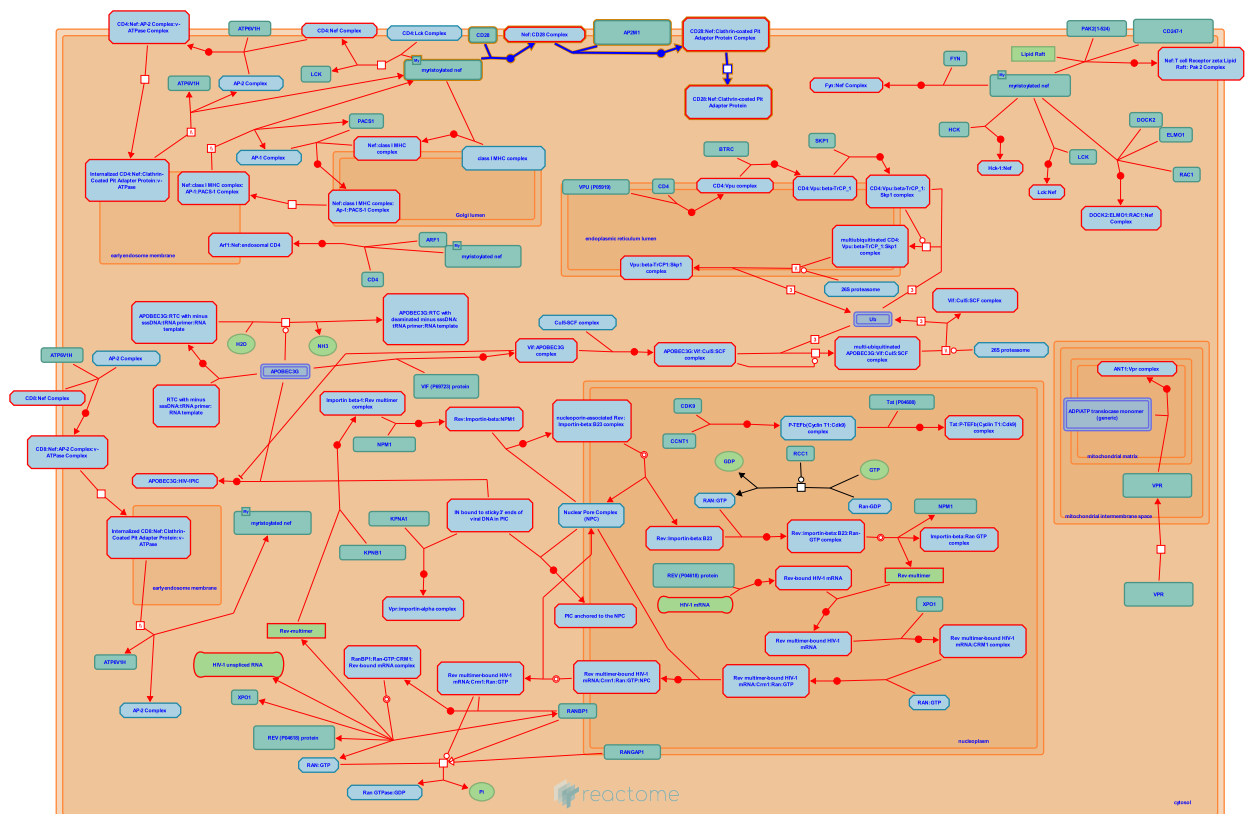


Nef mediated downregulation of CD28 cell surface expression



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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](https://reactome.org/about/reactome-textbook/).

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

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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. [↗](#)

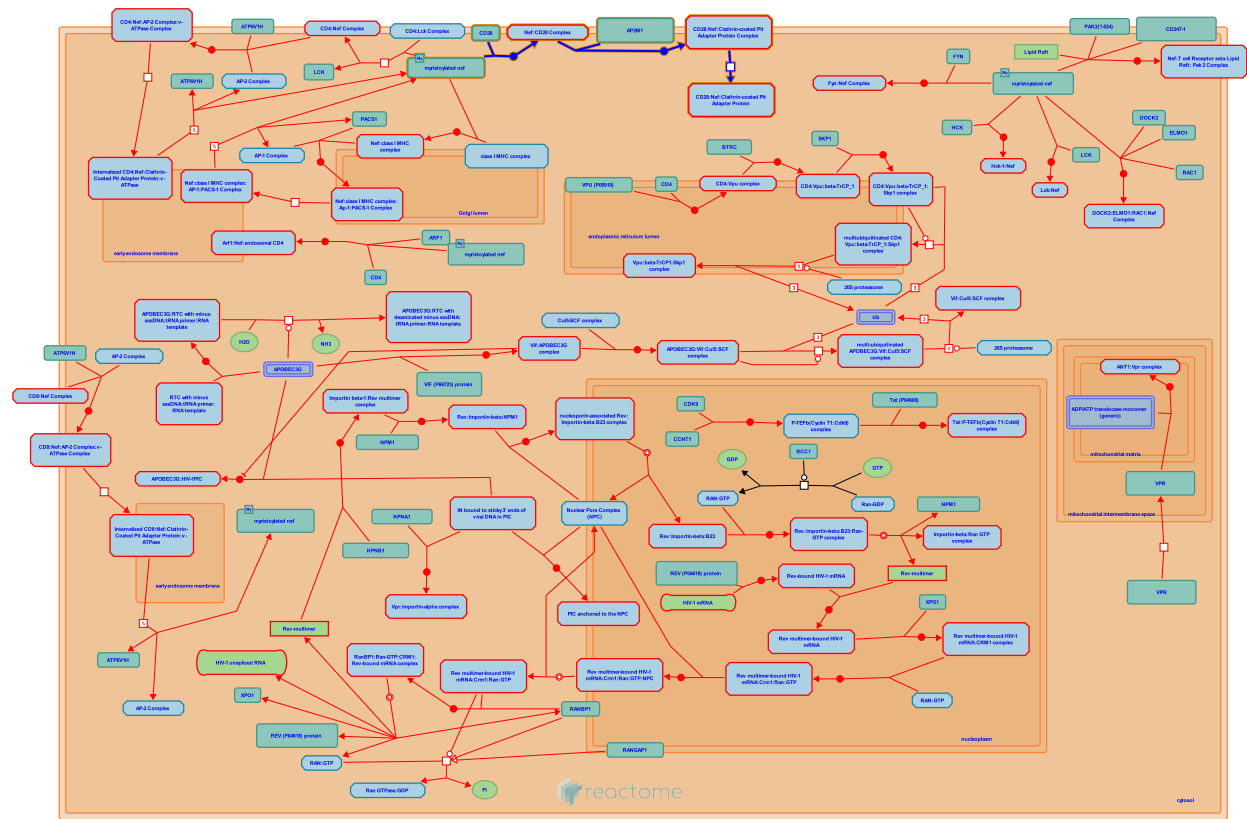
Reactome database release: 88

This document contains 1 pathway and 3 reactions ([see Table of Contents](#))

Nef mediated downregulation of CD28 cell surface expression ↗

Stable identifier: R-HSA-164939

Diseases: Human immunodeficiency virus infectious disease



Down-regulation of CD28 receptors involves a dileucine-based motif in the second disordered loop of Nef, which connects Nef to adaptor protein (AP) complex, which is a part of cellular endocytosis machinery. Nef induces accelerated endocytosis of CD28 via clathrin-coated pits followed by lysosomal degradation.

Literature references

Shohdy, N., Swigut, T., Skowronski, J. (2001). Mechanism for down-regulation of CD28 by Nef. *EMBO J*, 20, 1593-604.

Editions

2007-07-25	Authored	Gillespie, ME.
2007-08-07	Reviewed	Skowronski, J.

Formation of Nef CD28 cytoplasmic tail complex ↗

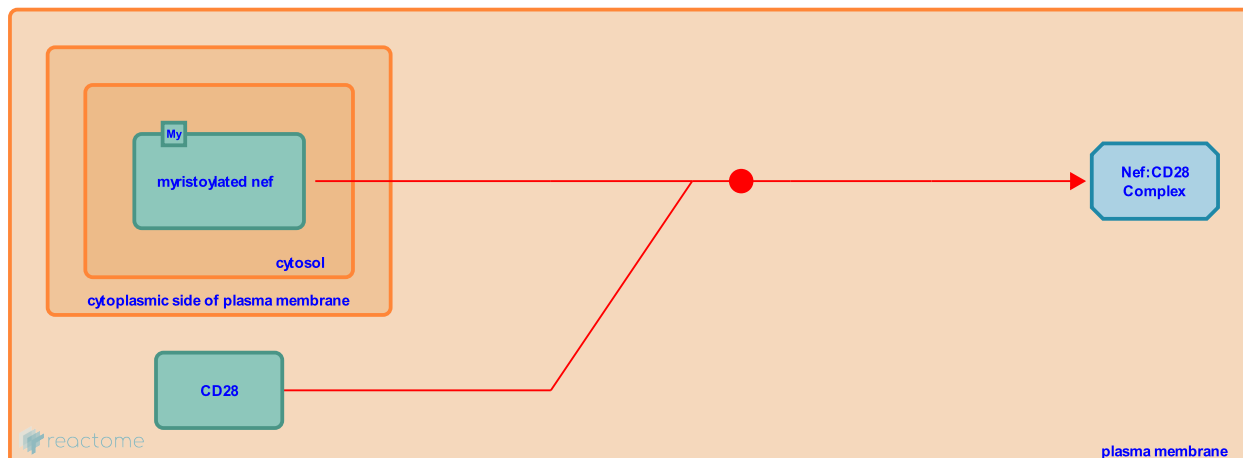
Location: [Nef mediated downregulation of CD28 cell surface expression](#)

Stable identifier: R-HSA-167630

Type: binding

Compartments: plasma membrane, cytosol

Diseases: Human immunodeficiency virus infectious disease



Down-regulation of CD28 receptors involves a dileucine-based motif in the second disordered loop of Nef, which connects Nef to adaptor protein (AP) complex, which is a part of cellular endocytosis machinery.

Followed by: [Formation of Nef:CD28:Clathrin-coated Pit Adapter Protein complex](#)

Literature references

Shohdy, N., Swigut, T., Skowronski, J. (2001). Mechanism for down-regulation of CD28 by Nef. *EMBO J*, 20, 1593-604.

↗

Editions

2007-07-25	Authored	Gillespie, ME.
2007-08-07	Reviewed	Skowronski, J.

Formation of Nef:CD28:Clathrin-coated Pit Adapter Protein complex ↗

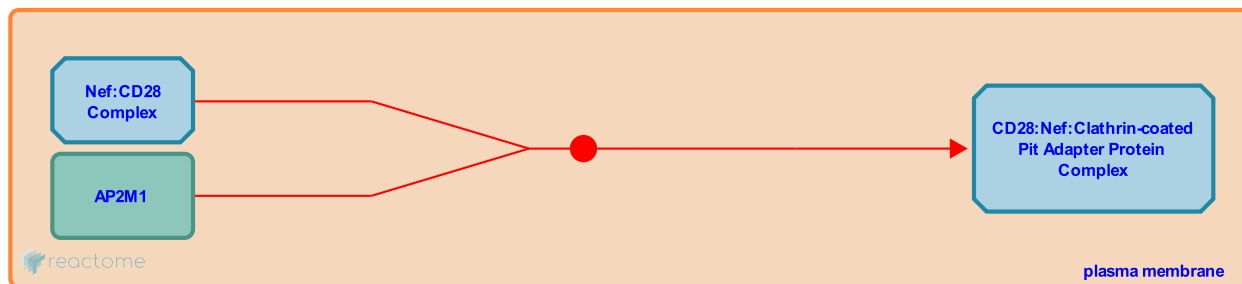
Location: [Nef mediated downregulation of CD28 cell surface expression](#)

Stable identifier: R-HSA-167633

Type: binding

Compartments: plasma membrane, cytosol

Diseases: Human immunodeficiency virus infectious disease



Nef induces accelerated endocytosis of CD28 via clathrin-coated pits.

Preceded by: [Formation of Nef CD28 cytoplasmic tail complex](#)

Followed by: [Internalization of Nef:CD28:Clathrin-Coated Pit Adapter Protein Complex](#)

Literature references

Shohdy, N., Swigut, T., Skowronski, J. (2001). Mechanism for down-regulation of CD28 by Nef. *EMBO J*, 20, 1593-604. ↗

Editions

2007-07-25	Authored	Gillespie, ME.
2007-08-07	Reviewed	Skowronski, J.

Internalization of Nef:CD28:Clathrin-Coated Pit Adapter Protein Complex [↗](#)

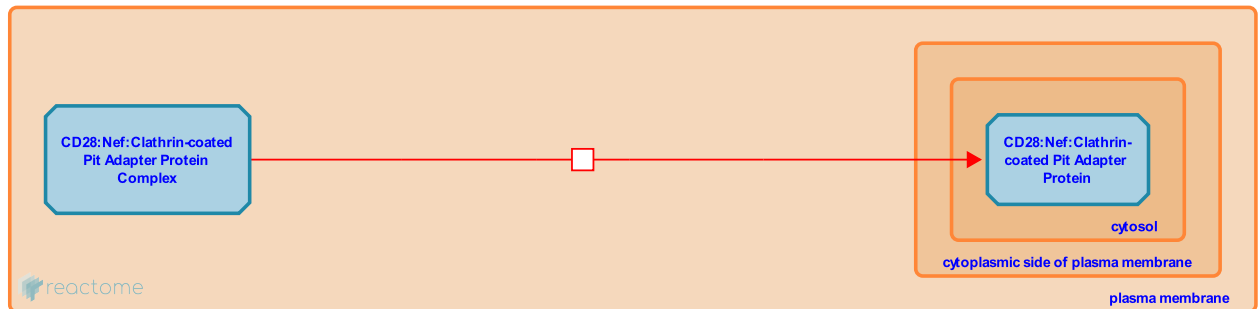
Location: [Nef mediated downregulation of CD28 cell surface expression](#)

Stable identifier: R-HSA-167637

Type: transition

Compartments: plasma membrane, cytosol

Diseases: Human immunodeficiency virus infectious disease



Once Nef has induced endocytosis of CD28, CD28 containing vesicles are targeted for lysosomal degradation.

Preceded by: [Formation of Nef:CD28:Clathrin-coated Pit Adapter Protein complex](#)

Literature references

Shohdy, N., Swigut, T., Skowronski, J. (2001). Mechanism for down-regulation of CD28 by Nef. *EMBO J*, 20, 1593-604.

[↗](#)

Editions

2007-07-25	Authored	Gillespie, ME.
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