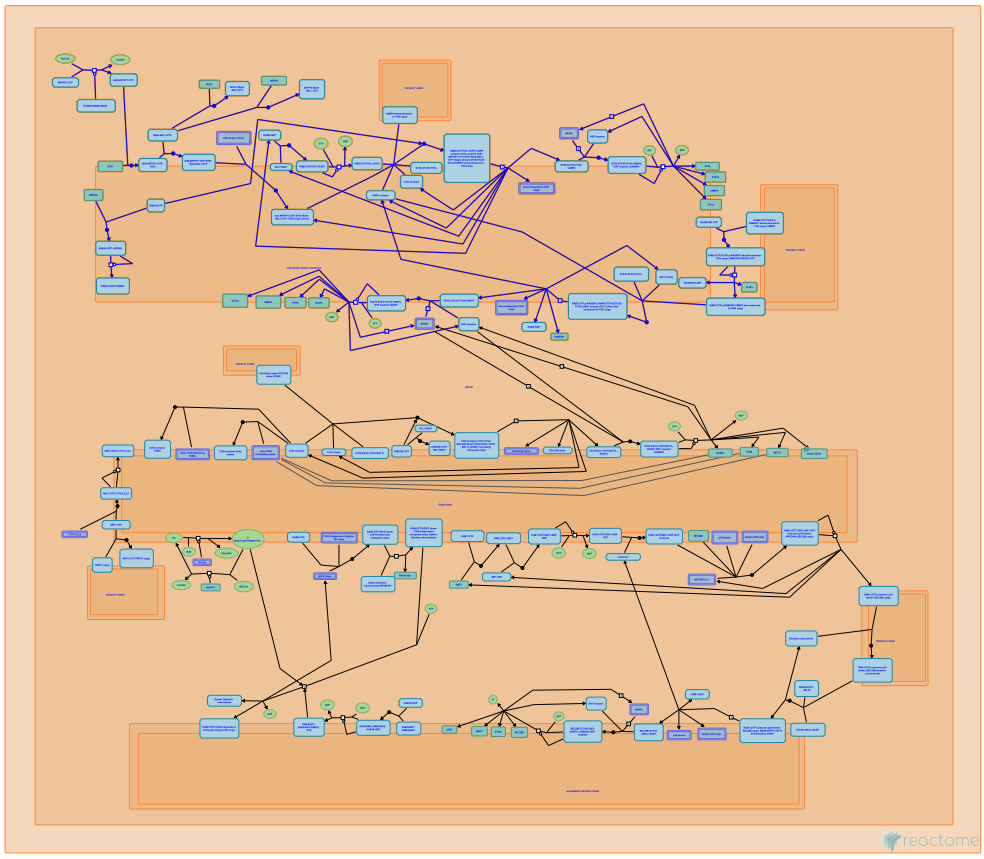
Retrograde transport at the Trans-Golgi-Network



Gillespie, ME., Rothfels, K.

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

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

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. ↗

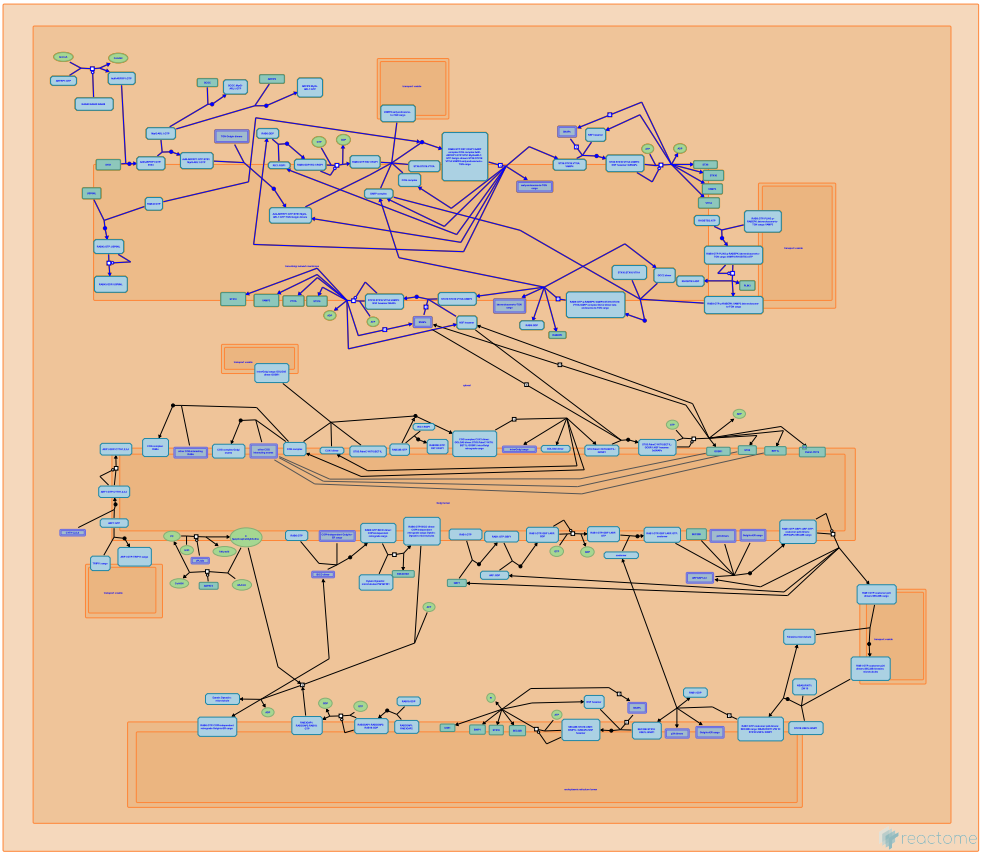
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Retrograde transport at the Trans-Golgi-Network ↗

Stable identifier: R-HSA-6811440



The trans-Golgi network is the docking site for retrograde cargo from the endolysosomal system and the plasma membrane. Typical cargo includes recycling resident TGN proteins such as TGOLN2 (also known as TGN46), receptors such as the mannose-6-phosphate receptors and toxins like Shiga, cholera and ricin which use the retrograde trafficking machinery to 'hitchhike' back through the secretory system for release into the cytoplasm (reviewed in Johannes and Popoff, 2008; Pfeffer, 2011; Sandvig et al, 2013). These cargo are trafficked from the endocytic system in a clathrin- and AP1-dependent manner that is described in more detail in the "Trans-Golgi network budding pathway" (just not yet). In general, it appears that vesicles are uncoated prior to their tethering and fusion at the TGN. At the TGN, at least 2 distinct tethering pathways exist. A RAB6-dependent pathway contributes to the fusion and docking of vesicles from the early endocytic pathway. These vesicles, which carry cargo such as TGOLN2 and toxins, dock at the TGN through interactions with TGN-localized Golgin tethers and with the multisubunit tethering complexes COG and GARP (reviewed in Bonafacino and Rojas, 2006; Bonafacino and Hierro, 2011; Pfeffer, 2011). In contrast, mannose-6-phosphate receptors appear to traffic from late endosomes to the TGN through a RAB9- and PLIN3-dependent pathway. Vesicles are recruited to the TGN through interaction of RAB9 with the atypical RHO GTPase RHOBTB3, and tethered by virtue of interaction with TGN-localized Golgins and the GARP complex (Perez-Victoria et al, 2008; Perez-Victoria et al, 2009; Diaz et al, 1999; reviewed in Pfeffer, 2011; Chia and Gleeson, 2014)

Literature references

Sandvig, K., Klokk, TI., Skotland, T., van Deurs, B. (2013). Retrograde transport of protein toxins through the Golgi apparatus. *Histochem. Cell Biol., 140,* 317-26. ↗

Hierro, A., Bonifacino, JS. (2011). Transport according to GARP: receiving retrograde cargo at the trans-Golgi network. *Trends Cell Biol., 21,* 159-67. ↗

Pfeffer, SR., Díaz, E. (1998). TIP47: a cargo selection device for mannose 6-phosphate receptor trafficking. *Cell, 93,* 433-43. ↗

Pfeffer, SR. (2011). Entry at the trans-face of the Golgi. *Cold Spring Harb Perspect Biol, 3.* ↗

Popoff, V., Johannes, L. (2008). Tracing the retrograde route in protein trafficking. *Cell, 135,* 1175-87. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

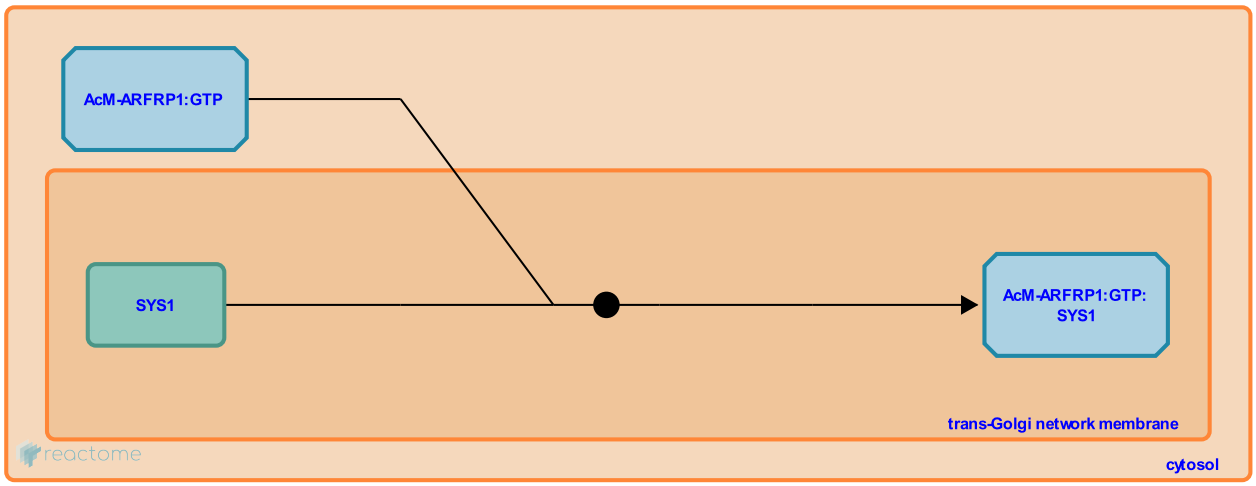
SYS1 binds AcM-ARFRP1 ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814088

Type: binding

Compartments: trans-Golgi network membrane



Acetylation of the N-terminal methionine of ARFRP1 contributes to its interaction with the Golgi-localized membrane protein SYS1. ARFRP1 is part of an ARF cascade at the late or trans-Golgi, where it plays a role in retrograde traffic by recruiting ARL1, which in turn interacts with a number of Golgin tethering factors required for vesicle docking at the TGN (Behnia et al, 2004; Setty et al, 2004; Shin et al, 2005; reviewed in Bonifacino and Rojas, 2006; Munro, 2011).

Preceded by: NatC acetylates ARFFRP1

Followed by: ARFRP1 recruits ARL1 to the TGN

Literature references

Rojas, R., Bonifacino, JS. (2006). Retrograde transport from endosomes to the trans-Golgi network. *Nat. Rev. Mol. Cell Biol., 7*, 568-79. ↗

Setty, SR., Boone, C., Tong, AH., Strochlic, TI., Burd, CG. (2004). Golgi targeting of ARF-like GTPase Arl3p requires its Nalpha-acetylation and the integral membrane protein Sys1p. *Nat. Cell Biol., 6*, 414-9. ↗

Panic, B., Whyte, JR., Behnia, R., Munro, S. (2004). Targeting of the Arf-like GTPase Arl3p to the Golgi requires N-terminal acetylation and the membrane protein Sys1p. *Nat. Cell Biol., 6*, 405-13. ↗

Uchiyama, Y., Kobayashi, H., Nakayama, K., Waguri, S., Kitamura, M., Suganuma, T. et al. (2005). Roles of ARFRP1 (ADP-ribosylation factor-related protein 1) in post-Golgi membrane trafficking. *J. Cell. Sci., 118*, 4039-48. ↗

Munro, S. (2011). The golgin coiled-coil proteins of the Golgi apparatus. *Cold Spring Harb Perspect Biol, 3*. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

NatC acetylates ARFFRP1 ↗

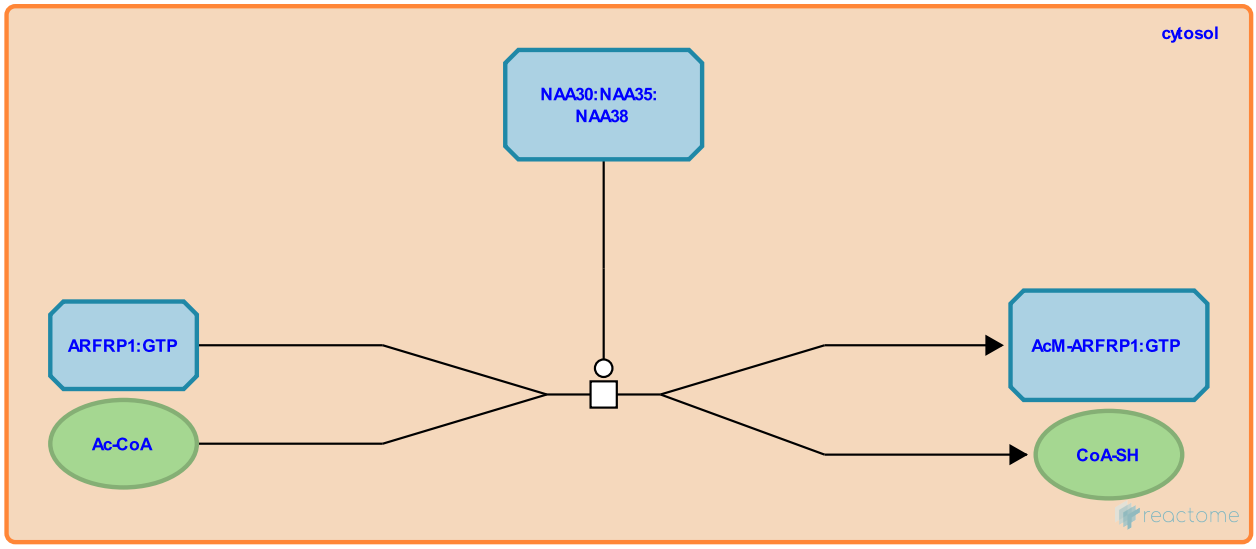
Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814090

Type: transition

Compartments: cytosol

Inferred from: NatC acetylates ARL3 (Saccharomyces cerevisiae)



ARFRP1 is an ARF family member GTPase that recruits ARL1 to the trans-Golgi network to play roles in retrograde trafficking of proteins from the endolysosomal system. ARFRP1 is an atypical ARF family member in that it is not myristolated, but is instead acetylated at the amino-terminal methionine by the NatC complex. Acetylation is required for the interaction of ARFRP1 with SYS1, which contributes to its targeting to its TGN (Behnia et al, 2004; Setty et al, 2004).

Followed by: SYS1 binds AcM-ARFRP1

Literature references

Setty, SR., Boone, C., Tong, AH., Strochlic, TI., Burd, CG. (2004). Golgi targeting of ARF-like GTPase Arl3p requires its Nalpha-acetylation and the integral membrane protein Sys1p. *Nat. Cell Biol., 6*, 414-9. ↗

Panic, B., Whyte, JR., Behnia, R., Munro, S. (2004). Targeting of the Arf-like GTPase Arl3p to the Golgi requires N-terminal acetylation and the membrane protein Sys1p. *Nat. Cell Biol., 6*, 405-13. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

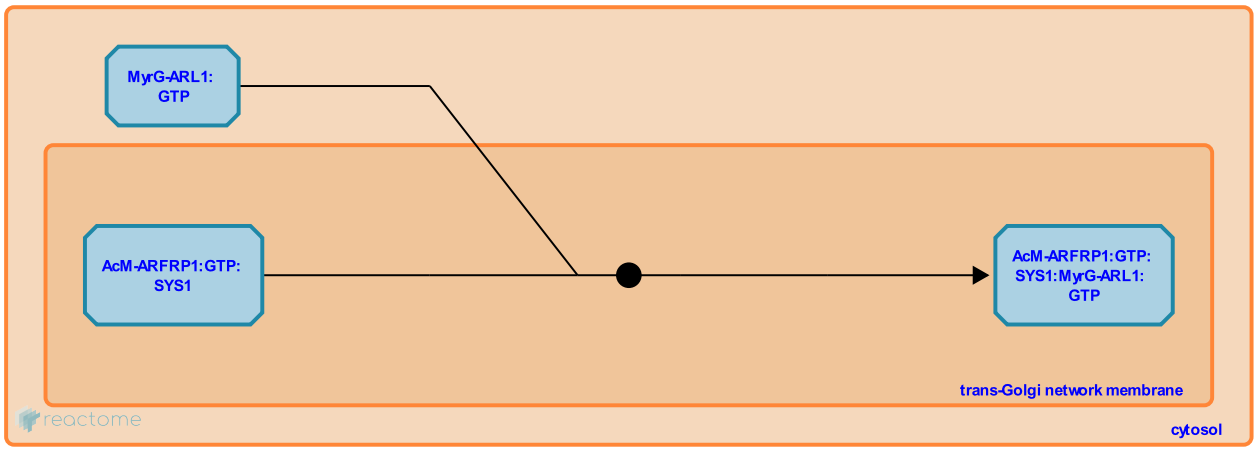
ARFRP1 recruits ARL1 to the TGN ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814086

Type: binding

Compartments: trans-Golgi network membrane



ARFRP1 regulates Golgi localization of ARL1, another ARF-like GTPase that itself recruits a number of Golgin-tethering factors to the TGN. Knockout strains of ARL3, the yeast homologue of ARFRP1, abrogates Golgi localization of both yeast Arl1p and the four yeast Golgin homologues, suggesting a cascade of ARL proteins is contributes to retrograde trafficking at the TGN (Setty et al, 2003; Setty et al, 2004; Behnia et al, 2004; Panic et al, 2003; reviewed in Munro, 2005; Bonafacino and Rojas, 2006). GEF and GAP proteins that regulate ARFRP1 and ARL1 activity have not yet been identified (reviewed in Munro, 2005).

Preceded by: SYS1 binds AcM-ARFRP1

Followed by: ARL1 recruits TGN Golgin homodimers

Literature references

Setty, SR., Marks, MS., Burd, CG., Shin, ME., Yoshino, A. (2003). Golgi recruitment of GRIP domain proteins by Arf-like GTPase 1 is regulated by Arf-like GTPase 3. *Curr. Biol., 13*, 401-4. ↗

Rojas, R., Bonifacino, JS. (2006). Retrograde transport from endosomes to the trans-Golgi network. *Nat. Rev. Mol. Cell Biol., 7*, 568-79. ↗

Setty, SR., Boone, C., Tong, AH., Strochlic, TI., Burd, CG. (2004). Golgi targeting of ARF-like GTPase Arl3p requires its Nalpha-acetylation and the integral membrane protein Sys1p. *Nat. Cell Biol., 6*, 414-9. ↗

Panic, B., Whyte, JR., Behnia, R., Munro, S. (2004). Targeting of the Arf-like GTPase Arl3p to the Golgi requires N-terminal acetylation and the membrane protein Sys1p. *Nat. Cell Biol., 6*, 405-13. ↗

Munro, S. (2005). The Arf-like GTPase Arl1 and its role in membrane traffic. *Biochem. Soc. Trans., 33*, 601-5. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

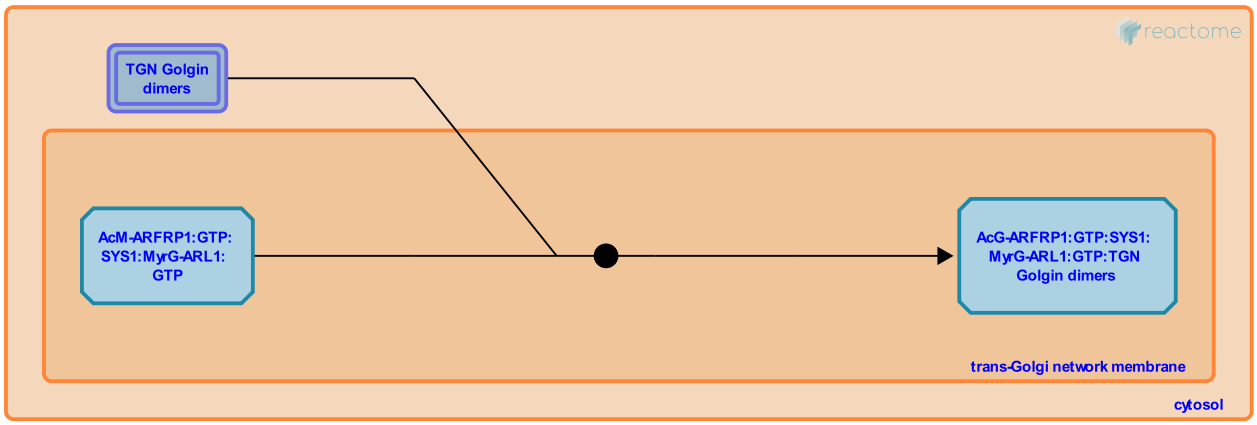
ARL1 recruits TGN Golgin homodimers ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814091

Type: binding

Compartments: trans-Golgi network membrane



GTP-bound ARL1, in conjunction with RAB6 and/or RAB9, is responsible for the recruitment of the 4 trans-Golgi network associated Golgin tethering factors, GOLGA4 (also known as Golgin245), GOLGA1 (also known as Golgin97), GCC1 (also known as GCC88) and GCC2 (also known as GCC185) (Barr et al, 1999; van Valkenburgh et al, 2001; Panic et al, 2003a; Panic et al, 2003b; Wu et al, 2004; Setty et al, 2003; reviewed in Munro et al, 2011). These coiled-coil tethering factors act as homodimers and participate in the recruitment of early endolysosomal-derived vesicles to the TGN by virtue of interacting with SNAREs and RAB proteins (Luke et al 2005; Lieu et al, 2007; Burguette et al, 2008; Ganley et al, 2008; Hayes et al, 2009; reviewed in Munro et al, 2011; Pfeffer, 2011). Evidence suggests that the Golgin tethering proteins show specificity for different retrograde cargos. For instance, retrograde transport of Shiga toxin requires both GOLGA1 and GOLGA4, while GOLGA1 is dispensible for transport of mannose-6-phosphate receptors (Lu et al, 2004; Yoshino et al, 2005; Reddy et al, 2006). Similarly, GCC1, but not GCC2, is required for TGN46 retrograde transport (Lieu et al, 2007; Derby et al, 2007). A fifth TGN-localized Golgin, TMF1, may also function similarly in retrograde transport from the early endosomes as it has been shown to interact with RAB6 and to be required for retrograde transport of Shiga toxin (Fridmann-Sirkis et al, 2004; Yamane et al, 2007).

Preceded by: ARFRP1 recruits ARL1 to the TGN

Literature references

Pfeffer, SR., Espinosa, E., Ganley, IG. (2008). A syntaxin 10-SNARE complex distinguishes two distinct transport routes from endosomes to the trans-Golgi in human cells. *J. Cell Biol., 180*, 159-72. ↗

Brown, FC., Hayes, GL., Nottingham, RM., Barr, FA., Haas, AK., Pfeffer, SR. (2009). Multiple Rab GTPase binding sites in GCC185 suggest a model for vesicle tethering at the trans-Golgi. *Mol. Biol. Cell, 20*, 209-17. ↗

Söllner, TH., Ravazzola, M., Orci, L., Amherdt, M., Rothman, JE., Tempst, P. et al. (1996). A v-SNARE implicated in intra-Golgi transport. *J. Cell Biol., 133*, 507-16. ↗

Burguete, AS., Pfeffer, SR., Fenn, TD., Brunger, AT. (2008). Rab and Arl GTPase family members cooperate in the localization of the golgin GCC185. *Cell, 132*, 286-98. ↗

Luke, MR., Perugini, MA., Houghton, F., Gleeson, PA. (2005). The trans-Golgi network GRIP-domain proteins form alpha-helical homodimers. *Biochem. J., 388*, 835-41. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

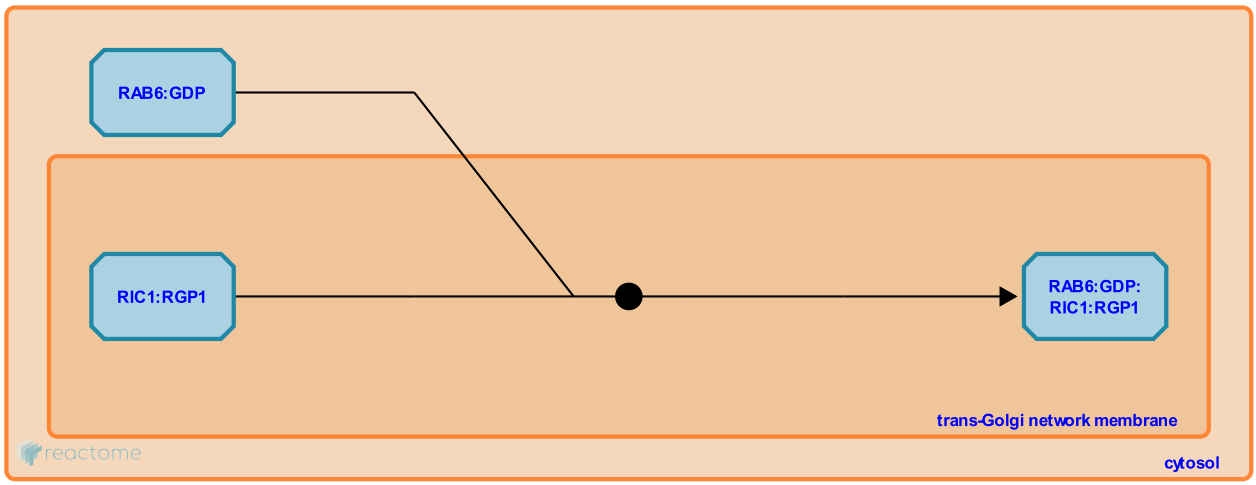
RIC1:RGP1 recruits RAB6:GDP to the TGN ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6811428

Type: binding

Compartments: trans-Golgi network membrane



RAB proteins are required for the RINT-1/ZW10 and COG-dependent organization of the Golgi ribbon stack, and for the trafficking of proteins through the Golgi. Indeed, cargo traffic through the Golgi depends on the maintenance of the Golgi stacks (Hirose et al, 2004; Arasaki et al, 2006; Sun et al, 2007; reviewed in Liu and Storrie, 2015). RAB6 is the primary RAB protein involved in intra-Golgi trafficking; it also has roles in COPI-independent retrograde traffic from the Golgi to the ER. RAB6A is a widely expressed isoform, while RAB6B is restricted to neuronal tissue (Darchen and Goud, 2000). RAB6 is localized to the trans-Golgi network (TGN), and a GTP-locked constitutively active form induces concentration of Golgi enzymes into the ER (Ferrano et al, 2104; Jiang and Storrie, 2005; Martinex et al, 1997; Micaroni et al, 2013; Storrie et al, 2012; Sun et al, 2007; Young et al, 2005). Inactive RAB6:GDP is recruited to the TGN through interaction with the RIC1:RGP1 complex, which also acts as a guanine nucleotide exchange factor (GEF) for RAB6 (Pusapati et al, 2012; Siniossoglou et al, 2000; Siniossoglou et al, 2001).

Followed by: RIC1:RGP1 stimulates nucleotide RAB6 nucleotide exchange

Literature references

Ketteler, R., Burden, JJ., Martin-Martin, B., Knight, AE., Dyer, CE., Westmoreland, D. et al. (2014). A two-tier Golgi-based control of organelle size underpins the functional plasticity of endothelial cells. *Dev. Cell, 29*, 292-304. ↗

Tagaya, M., Hatsuzawa, K., Takio, K., Tohyama, M., Tani, K., Hirose, H. et al. (2004). Implication of ZW10 in membrane trafficking between the endoplasmic reticulum and Golgi. *EMBO J., 23*, 1267-78. ↗

Pelham, HR., Siniossoglou, S. (2001). An effector of Ypt6p binds the SNARE Tlg1p and mediates selective fusion of vesicles with late Golgi membranes. *EMBO J., 20*, 5991-8. ↗

Pelham, HR., Siniossoglou, S., Peak-Chew, SY. (2000). Ric1p and Rgp1p form a complex that catalyses nucleotide exchange on Ypt6p. *EMBO J., 19*, 4885-94. ↗

Morgan, GP., Jones, N., Micaroni, M., Pan, TH., Kamykowski, JA., Marsh, BJ. et al. (2012). Electron tomography reveals Rab6 is essential to the trafficking of trans-Golgi clathrin and COPI-coated vesicles and the maintenance of Golgi cisternal number. *Traffic, 13*, 727-44. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

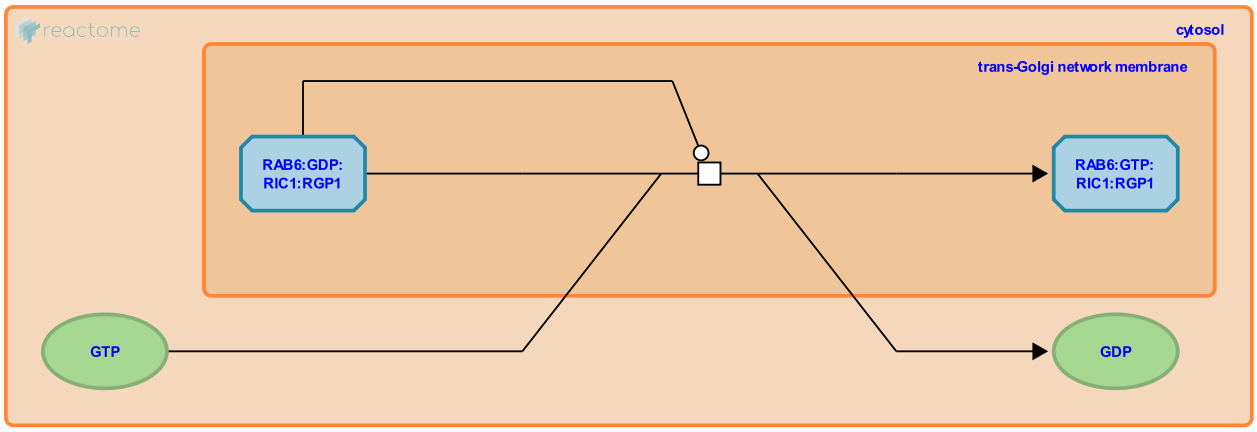
RIC1:RGP1 stimulates nucleotide RAB6 nucleotide exchange ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6811429

Type: transition

Compartments: trans-Golgi network membrane



The RIC1:RGP1 complex stimulates nucleotide exchange on trans-Golgi network (TGN)-localized RAB6, activating it (Pusapati et al, 2012; Siniossoglou et al 2001; Siniossoglou et al, 2000). Acitvated RAB6 nucleates a tethering complex at the TGN that is required for fusion of endosome-derived vesicles arriving at the late Golgi (Siniossoglou et al, 2001; Liewen et al, 2005; Perez-Victoria et al, 2008; Perez-Victoria et al, 2009; reviewed in Bonaficino and Hierro, 2011).

Preceded by: RIC1:RGP1 recruits RAB6:GDP to the TGN

Followed by: RAB6:GTP binds the GARP and COG complexes, t-SNAREs and endosome-derived vesicles

Literature references

Mardones, GA., Pérez-Victoria, FJ., Bonifacino, JS. (2008). Requirement of the human GARP complex for mannose 6-phosphate-receptor-dependent sorting of cathepsin D to lysosomes. *Mol. Biol. Cell, 19*, 2350-62. ↗

Pelham, HR., Siniossoglou, S. (2001). An effector of Ypt6p binds the SNARE Tlg1p and mediates selective fusion of vesicles with late Golgi membranes. *EMBO J., 20*, 5991-8. ↗

Pfeffer, SR., Luchetti, G., Pusapati, GV. (2012). Ric1-Rgp1 complex is a guanine nucleotide exchange factor for the late Golgi Rab6A GTPase and an effector of the medial Golgi Rab33B GTPase. *J. Biol. Chem., 287*, 42129-37. ↗

Pérez-Victoria, FJ., Bonifacino, JS. (2009). Dual roles of the mammalian GARP complex in tethering and SNARE complex assembly at the trans-golgi network. *Mol. Cell. Biol., 29*, 5251-63. ↗

Pelham, HR., Siniossoglou, S., Peak-Chew, SY. (2000). Ric1p and Rgp1p form a complex that catalyses nucleotide exchange on Ypt6p. *EMBO J., 19*, 4885-94. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

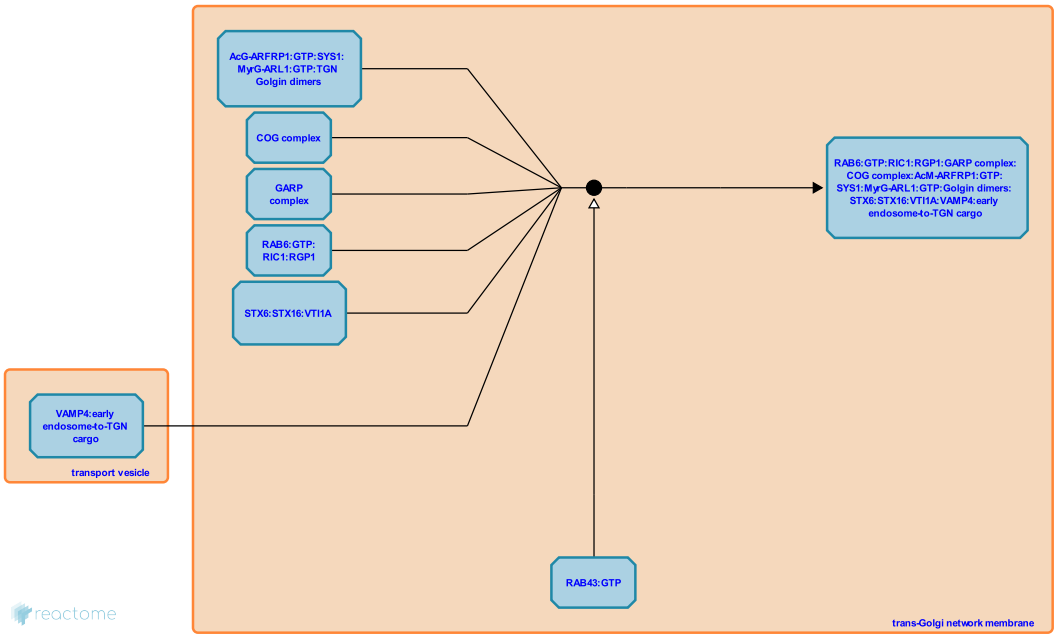
RAB6:GTP binds the GARP and COG complexes, t-SNAREs and endosome-derived vesicles ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6811431

Type: binding

Compartments: trans-Golgi network membrane



Active RAB6 contributes to the recruitment of the Golgi-associated retrograde protein (GARP) tethering complex to the TGN, where it aids in the capture of retrograde vesicles from the early endosome (Liewen et al, 2005; reviewed in Bonifacino and Hierro, 2011). Typical cargo of these vesicles includes resident TGN proteins such as TGOLN2 (also known as TGN46) and internalized Shiga toxin subunit B (STx-B) and cholera toxin (Perez-Victoria et al, 2008; Ganley et al 2008; Pusapati et al, 2012; reviewed in Pfeffer, 2011; Liu and Storrie, 2012). Two studies have identifed RAB43 and its associated GAP USP6NL as being required for the retrograde traffic of Shiga toxin, however the details of this remain to be worked out (Haas et al, 2007; Fuchs et al, 2007).
The human GARP complex consists of VPS54, VPS53, VPS52 and VPS51 and has been shown to interact with GTP-bound RAB6, with the TGN SNAREs STX10 and STX16 and with a vesicle fraction containing the v-SNARE VAMP4 (Connibear et al, 2000; Liewen et al, 2005; Perez-Victoria et al, 2009; Perez-Victoria et al, 2010; Siniossoglou and Pelham, 2002; reviewed in Bonafacino and Hierro, 2011).

Like the GARP complex, the conserved oligomeric Golgi (COG) complex has also been implicated in retrograde traffic of TGOLN2 and STx-B in a STX6:STX16:VTI1A and VAMP4-dependent manner, and COG has been shown to interact directly with RAB6 (Mallard et al, 2002; Fukuda et al, 2008; Laufman et al, 2011; reviewed in Pfeffer, 2011). Despite the representation in this reaction, however, there is not yet evidence that the GARP and the COG complexes act together to facilitate the capture of a single early endosome-derived vesicle.
In addition to the multisubunit tethering complexes COG and GARP, the long coiled-coil TGN-associated Golgins also contribute to tethering of vesicles derived from the early endosome (Luke et al, 2005; Derby et al, 2007; Reddy et al, 2006; Lu et al, 2004; Yoshino et al, 2005; Hayes et al, 2009; reviewed in Munro, 2011).

Preceded by: RIC1:RGP1 stimulates nucleotide RAB6 nucleotide exchange

Followed by: Fusion of early-endosome derived vesicles at the TGN

Literature references

Hong, W., Lev, S., Laufman, O. (2011). The COG complex interacts directly with Syntaxin 6 and positively regulates endosome-to-TGN retrograde transport. *J. Cell Biol., 194*, 459-72. ↗

Pfeffer, SR., Espinosa, E., Ganley, IG. (2008). A syntaxin 10-SNARE complex distinguishes two distinct transport routes from endosomes to the trans-Golgi in human cells. *J. Cell Biol., 180*, 159-72. ↗

Brown, FC., Hayes, GL., Nottingham, RM., Barr, FA., Haas, AK., Pfeffer, SR. (2009). Multiple Rab GTPase binding sites in GCC185 suggest a model for vesicle tethering at the trans-Golgi. *Mol. Biol. Cell, 20*, 209-17. ↗

Yue, X., Galli, T., Hong, W., Saint-Pol, A., Johannes, L., Tenza, D. et al. (2002). Early/recycling endosomes-to-TGN transport involves two SNARE complexes and a Rab6 isoform. *J. Cell Biol., 156*, 653-64. ↗

Luke, MR., Perugini, MA., Houghton, F., Gleeson, PA. (2005). The trans-Golgi network GRIP-domain proteins form alpha-helical homodimers. *Biochem. J., 388*, 835-41. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

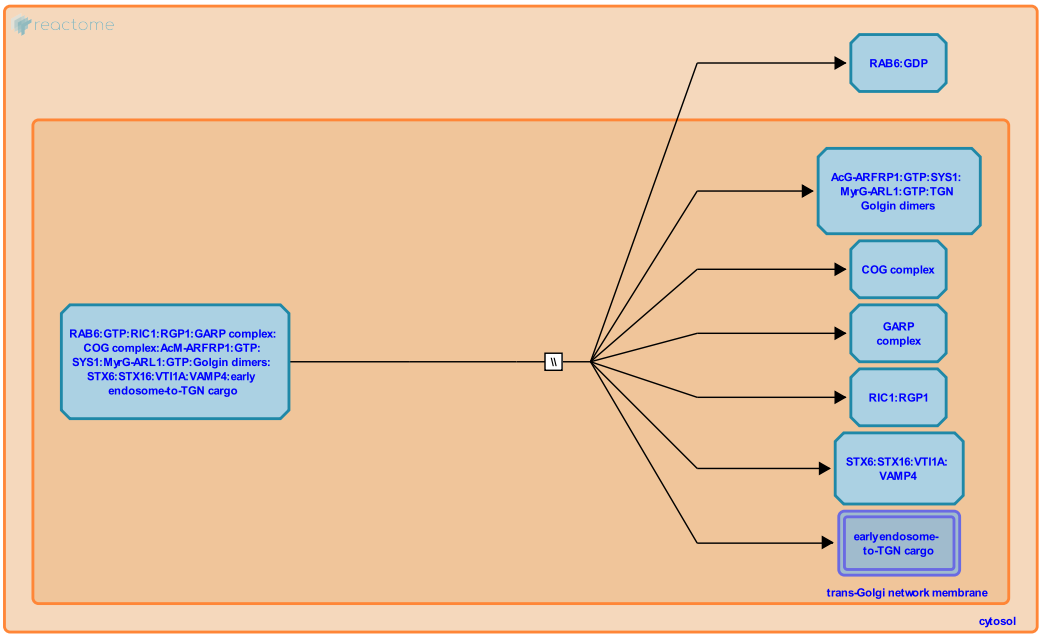
Fusion of early-endosome derived vesicles at the TGN ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814682

Type: omitted

Compartments: trans-Golgi network membrane



After capture at the trans-Golgi network by SNAREs and tethering factors, early endosome-derived vesicles undergo membrane fusion, delivering cargo and the cis-SNARE complex to the TGN membrane. The details of this fusion event are not fully established (reviewed in Pfeffer, 2011).

Preceded by: RAB6:GTP binds the GARP and COG complexes, t-SNAREs and endosome-derived vesicles

Followed by: cis-SNARE binds SNAPs and NSF hexamer at the TGN

Literature references

Pfeffer, SR. (2011). Entry at the trans-face of the Golgi. *Cold Spring Harb Perspect Biol, 3.* ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

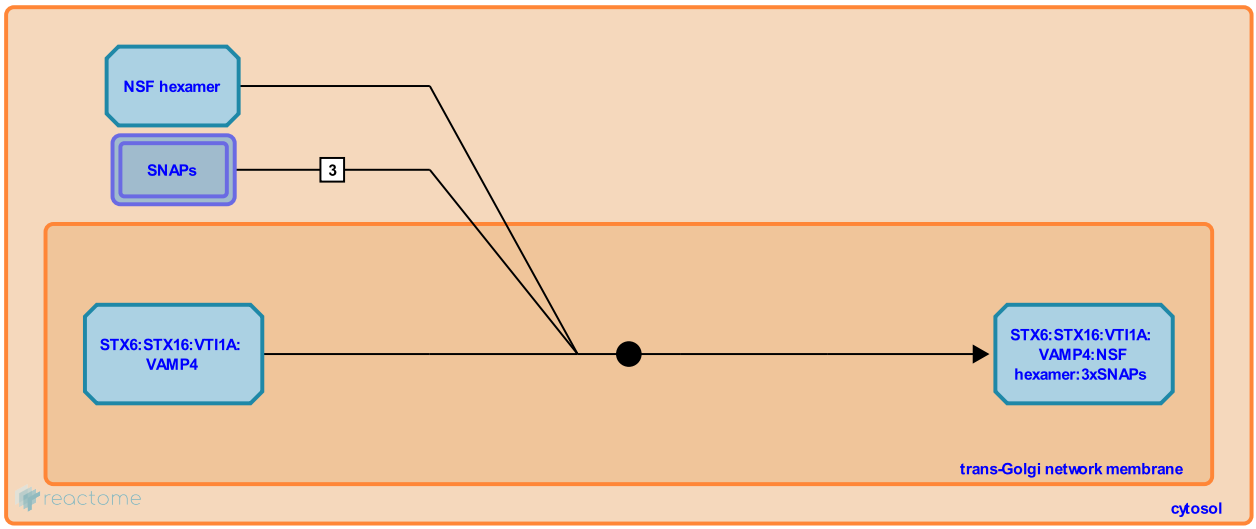
cis-SNARE binds SNAPs and NSF hexamer at the TGN ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814684

Type: binding

Compartments: trans-Golgi network membrane



After membrane fusion, the 4-membered cis-SNARE complex is dissociated in an ATP-dependent manner by SNAP and NSF (Mayer et al, 1996; Sollner et al, 1993; reviewed in Jahn and Scheller, 2006; Sudhof and Rothman, 2009).

Preceded by: Fusion of early-endosome derived vesicles at the TGN

Followed by: NSF-dependent ATP hydrolysis disassembles the cis-SNARE at the TGN

Literature references

Haas, A., Mayer, A., Wickner, W. (1996). Sec18p (NSF)-driven release of Sec17p (alpha-SNAP) can precede docking and fusion of yeast vacuoles. *Cell, 85*, 83-94. ↗

Söllner, T., Whiteheart, SW., Scheller, RH., Bennett, MK., Rothman, JE. (1993). A protein assembly-disassembly pathway in vitro that may correspond to sequential steps of synaptic vesicle docking, activation, and fusion. *Cell, 75*, 409-18. ↗

Südhof, TC., Rothman, JE. (2009). Membrane fusion: grappling with SNARE and SM proteins. *Science, 323*, 474-7. ↗

Scheller, RH., Jahn, R. (2006). SNAREs--engines for membrane fusion. *Nat. Rev. Mol. Cell Biol., 7*, 631-43. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

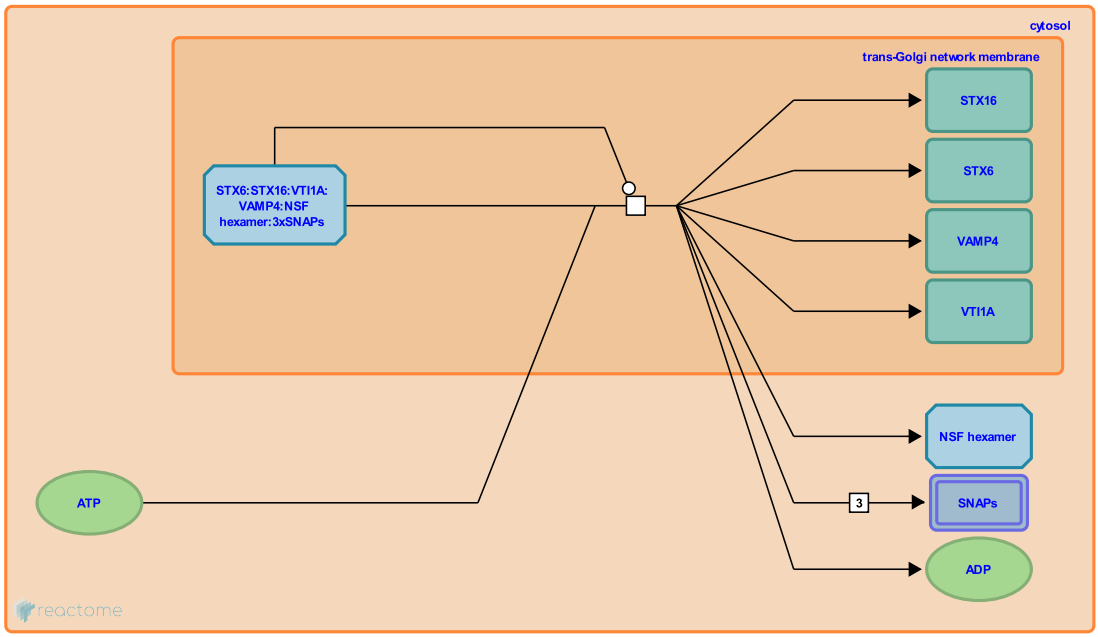
NSF-dependent ATP hydrolysis disassembles the cis-SNARE at the TGN

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814683

Type: transition

Compartments: trans-Golgi network membrane



NSF-dependent hydrolysis of ATP is required to disassociate the cis-SNARE complex, releasing the SNAREs for further rounds of membrane fusion (Mayer et al, 1996; Muller et al, 1999; Muller et al, 2002; Otto et al, 1997; Whiteheart et al, 2004; Yu et al, 1999; Zhao et al, 2012; Shah et al, 2015; reviewed in Sudhof and Rothman, 2009).

Preceded by: cis-SNARE binds SNAPs and NSF hexamer at the TGN

Literature references

Haas, A., Mayer, A., Wickner, W. (1996). Sec18p (NSF)-driven release of Sec17p (alpha-SNAP) can precede docking and fusion of yeast vacuoles. *Cell, 85*, 83-94.

Hanson, PI., Jahn, R., Otto, H. (1997). Assembly and disassembly of a ternary complex of synaptobrevin, syntaxin, and SNAP-25 in the membrane of synaptic vesicles. *Proc. Natl. Acad. Sci. U.S.A., 94*, 6197-201.

Yu, RC., Jahn, R., Brunger, AT. (1999). NSF N-terminal domain crystal structure: models of NSF function. *Mol. Cell, 4*, 97-107.

Matveeva, EA., Whiteheart, SW. (2004). Multiple binding proteins suggest diverse functions for the N-ethylmaleimide sensitive factor. *J. Struct. Biol., 146*, 32-43.

Südhof, TC., Rothman, JE. (2009). Membrane fusion: grappling with SNARE and SM proteins. *Science, 323*, 474-7.

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

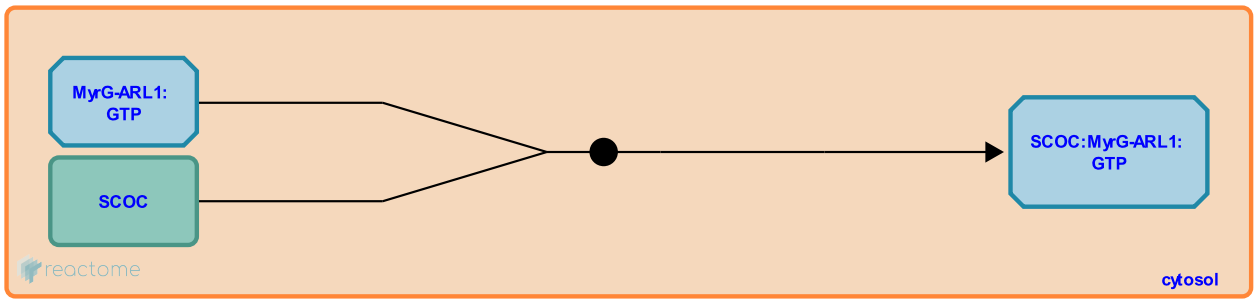
ARL1:GTP binds SCOC ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814096

Type: binding

Compartments: cytosol



Two hybrid screening with human ARL1 as bait identified SCOC as a novel ARL1:GTP-interacting partner (Van Valkenburgh et al, 2001). SCOC (short coiled coil) shares 26% identity and 51% homology with GOLGA2, binds ARL1:GTPagamma S as assessed by affinity chromatography and shows extensive colocalization wtih beta-COP and ARL1 at the Golgi, however the role of this complex is not known (Van Valkenburgh et al, 2001). SCOC is also known to play roles in autophagy, as part of a complex with FEZ1 (McKnight et al, 2012; reviewed in Joachim et al, 2012).

Literature references

Tooze, SA., Alemu, EA., Jefferies, HB., Johansen, T., McKnight, NC., Howell, M. et al. (2012). Genome-wide siRNA screen reveals amino acid starvation-induced autophagy requires SCOC and WAC. *EMBO J., 31*, 1931-46. ↗

Sharer, JD., Zhu, X., Kahn, RA., Van Valkenburgh, H., Shern, JF. (2001). ADP-ribosylation factors (ARFs) and ARF-like 1 (ARL1) have both specific and shared effectors: characterizing ARL1-binding proteins. *J. Biol. Chem., 276*, 22826-37. ↗

Tooze, SA., Joachim, J., McKnight, NC., Wirth, M. (2012). Coiling up with SCOC and WAC: two new regulators of starvation-induced autophagy. *Autophagy, 8*, 1397-400. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

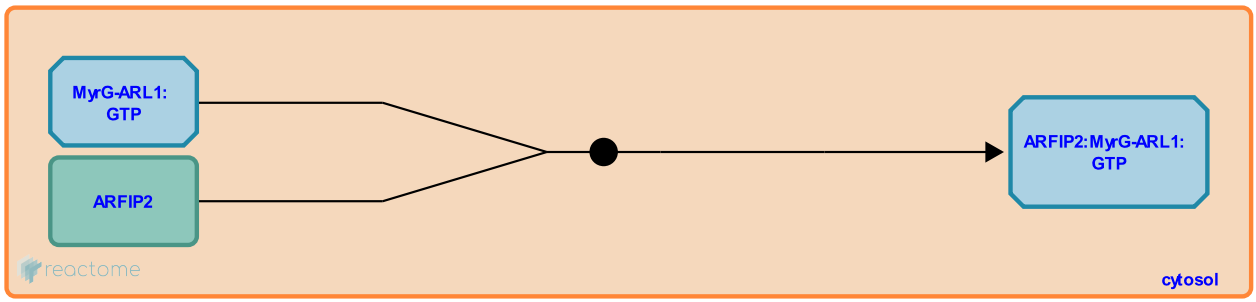
ARL1:GTP binds ARFIP2 ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814094

Type: binding

Compartments: cytosol



Two hybrid screening with human ARL1 as bait identified ARFIP2 as a novel ARL1:GTP-interacting partner (Van Valkenburgh et al, 2001). Interaction between ARFIP2 and ARL1 increases the amount of ARL1:GTP four-fold , although the significance of this is not clear (Van Vlakenburgh et al, 2001). ARFIP2 is also known to interact with RAC1 and to influence membrane ruffling (van Aelst et al, 1996; Tarricone et al, 2001)

Literature references

Justin, N., Rittinger, K., Walker, PA., Xiao, B., Smerdon, SJ., Gamblin, SJ. et al. (2001). The structural basis of Arfaptin-mediated cross-talk between Rac and Arf signalling pathways. *Nature, 411*, 215-9. ↗

Van Aelst, L., Joneson, T., Bar-Sagi, D. (1996). Identification of a novel Rac1-interacting protein involved in membrane ruffling. *EMBO J., 15*, 3778-86. ↗

Sharer, JD., Zhu, X., Kahn, RA., Van Valkenburgh, H., Shern, JF. (2001). ADP-ribosylation factors (ARFs) and ARF-like 1 (ARL1) have both specific and shared effectors: characterizing ARL1-binding proteins. *J. Biol. Chem., 276*, 22826-37. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

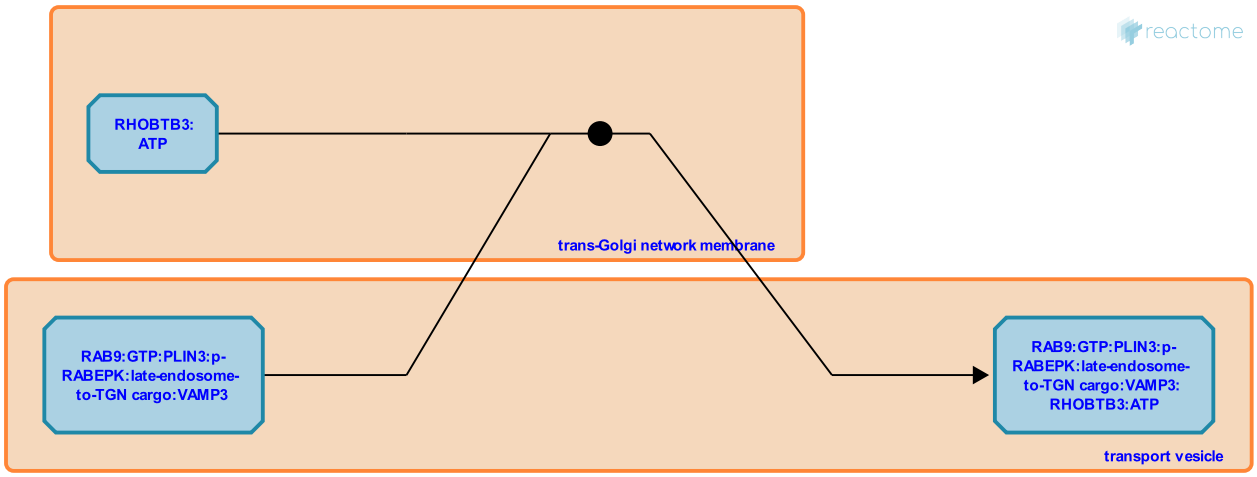
RAB9 binds RHOBTB3, bringing late endosome-derived vesicles to the TGN ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814675

Type: binding

Compartments: trans-Golgi network membrane



Retrograde traffic of mannose-6-phosphate receptors (M6PRs) from the late endosome depends on RAB9 (Lombardi et al, 1993; Riederer et al, 1994; Barbero et al, 2002; reviewed in Pfeffer, 2011). Cargo recognition at the late endosome is mediated by the RAB9-interacting protein PLIN3/TIP47, which concentrates retrograde cargo into VAMP3 RAB9 positive vesicles (Diaz et al, 1998; Carroll et al, 2001; Reddy et al, 2006; Ganley et al, 2008). RABEPK is another RAB9:GTP interacting protein that is required for retrograde transport of M6PR to the TGN (Diaz et al, 1997). At the trans-Golgi network, RAB9 and PILN3 interact with the atypical RHO GTPase related protein RHOBTB3. This interaction is required for the TGN-localization of RAB9 M6PR positive vesicles. Interaction of RAB9 with the C-terminal domain of RHOBTB3 relieves an inhibitory intramolecular interaction in RHOBTB3, allowing the N-terminal domain to achieve maximal ATP hydrolysis, which is thought to promote the release of PLIN3/TIP47 as a precursor to vesicle fusion at the TGN (Espinosa et al, 2009)

Followed by: ATP hydrolysis by RHOBTB3 promotes PLIN3 dissociation

Literature references

Pfeffer, SR., Díaz, E., Schimmöller, F. (1997). A novel Rab9 effector required for endosome-to-TGN transport. *J. Cell Biol., 138*, 283-90. ↗

Pfeffer, SR., Espinosa, E., Ganley, IG. (2008). A syntaxin 10-SNARE complex distinguishes two distinct transport routes from endosomes to the trans-Golgi in human cells. *J. Cell Biol., 180*, 159-72. ↗

Reddy, JV., Burguete, AS., Nottingham, RM., Sridevi, K., Pfeffer, SR., Ganley, IG. (2006). A functional role for the GCC185 golgin in mannose 6-phosphate receptor recycling. *Mol. Biol. Cell, 17*, 4353-63. ↗

Hanna, J., Barbero, P., Carroll, KS., Pfeffer, SR., Simon, I., Krise, J. (2001). Role of Rab9 GTPase in facilitating receptor recruitment by TIP47. *Science, 292*, 1373-6. ↗

Pfeffer, SR., Shapiro, AD., Riederer, MA., Soldati, T., Lin, J. (1994). Lysosome biogenesis requires Rab9 function and receptor recycling from endosomes to the trans-Golgi network. *J. Cell Biol., 125*, 573-82. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

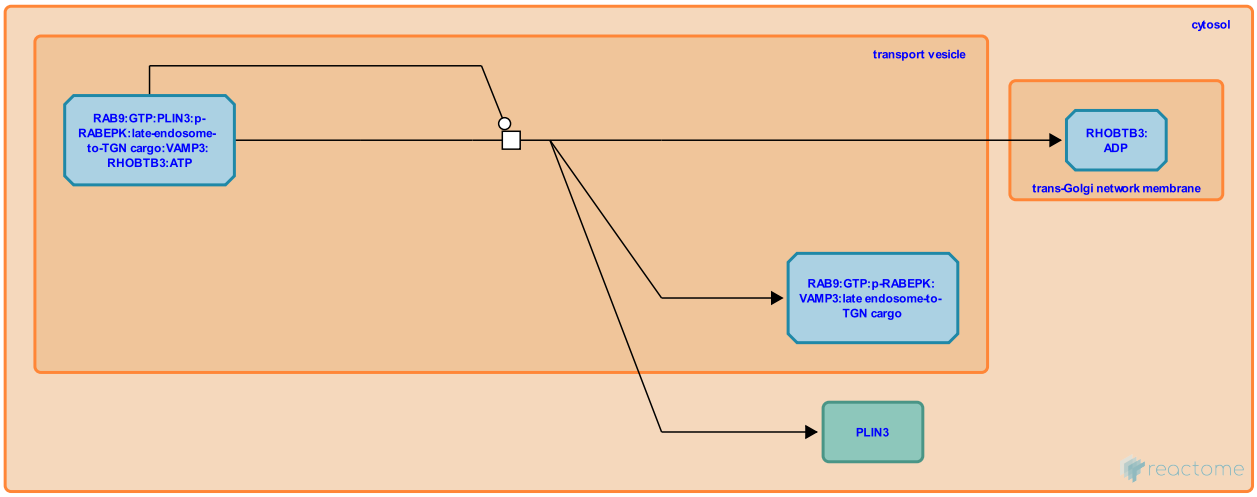
ATP hydrolysis by RHOBTB3 promotes PLIN3 dissociation ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814670

Type: transition

Compartments: transport vesicle



ATP hydrolysis by RHOBTB is thought to promote uncoating of the late endosome-derived vesicle, releasing PLIN3/TIP47 in preparation for vesicle fusion (Espinosa et al, 2009; reviewed in Pfeffer, 2011).

Preceded by: RAB9 binds RHOBTB3, bringing late endosome-derived vesicles to the TGN

Followed by: Tethering of late endosome-derived vesicles by GARP, STX10:ST16:VTI1A and Golgins

Literature references

Pfeffer, SR. (2011). Entry at the trans-face of the Golgi. *Cold Spring Harb Perspect Biol, 3.* ↗

Espinosa, EJ., Calero, M., Sridevi, K., Pfeffer, SR. (2009). RhoBTB3: a Rho GTPase-family ATPase required for endosome to Golgi transport. *Cell, 137*, 938-48. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

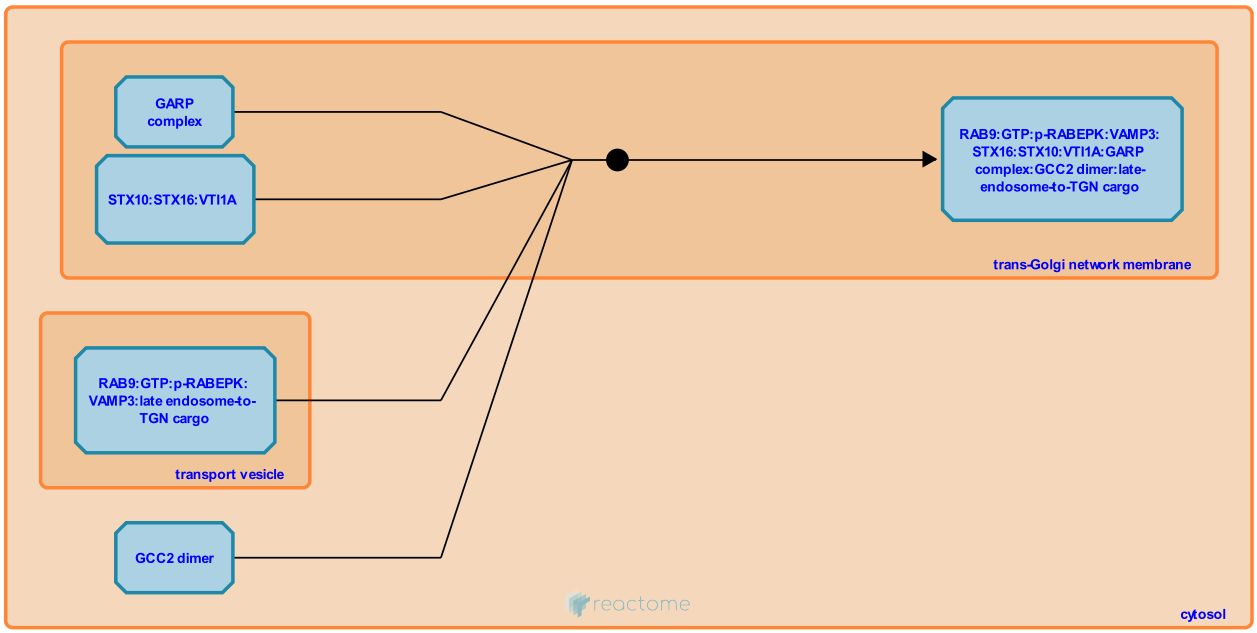
Tethering of late endosome-derived vesicles by GARP, STX10:ST16:VTI1A and Golgins

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814674

Type: binding

Compartments: trans-Golgi network membrane



RAB9 positive vesicles from the late endosomes are tethered at the trans-Golgi network (TGN) through interaction with the GARP complex, the TGN-specific Golgin GCC2 and a t-SNARE complex consisting of STX10, STX16 and VTI1A (Hayes et al, 2009; Derby et al, 2007; Reddy et al, 2006; Ganley et al, 2008; Perez-Victoria et al, 2009; Lombardi et al, 1993; Lieu et al, 2007; reviewed in Chia and Gleeson, 2014)

Preceded by: ATP hydrolysis by RHOBTB3 promotes PLIN3 dissociation

Followed by: Fusion of late-endosome derived vesicles at the TGN

Literature references

Pfeffer, SR., Espinosa, E., Ganley, IG. (2008). A syntaxin 10-SNARE complex distinguishes two distinct transport routes from endosomes to the trans-Golgi in human cells. *J. Cell Biol., 180*, 159-72.

Reddy, JV., Burguete, AS., Nottingham, RM., Sridevi, K., Pfeffer, SR., Ganley, IG. (2006). A functional role for the GCC185 golgin in mannose 6-phosphate receptor recycling. *Mol. Biol. Cell, 17*, 4353-63.

Brown, FC., Hayes, GL., Nottingham, RM., Barr, FA., Haas, AK., Pfeffer, SR. (2009). Multiple Rab GTPase binding sites in GCC185 suggest a model for vesicle tethering at the trans-Golgi. *Mol. Biol. Cell, 20*, 209-17.

Chia, PZ., Gleeson, PA. (2014). Membrane tethering. *F1000Prime Rep, 6*, 74.

Pérez-Victoria, FJ., Bonifacino, JS. (2009). Dual roles of the mammalian GARP complex in tethering and SNARE complex assembly at the trans-golgi network. *Mol. Cell. Biol., 29*, 5251-63.

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

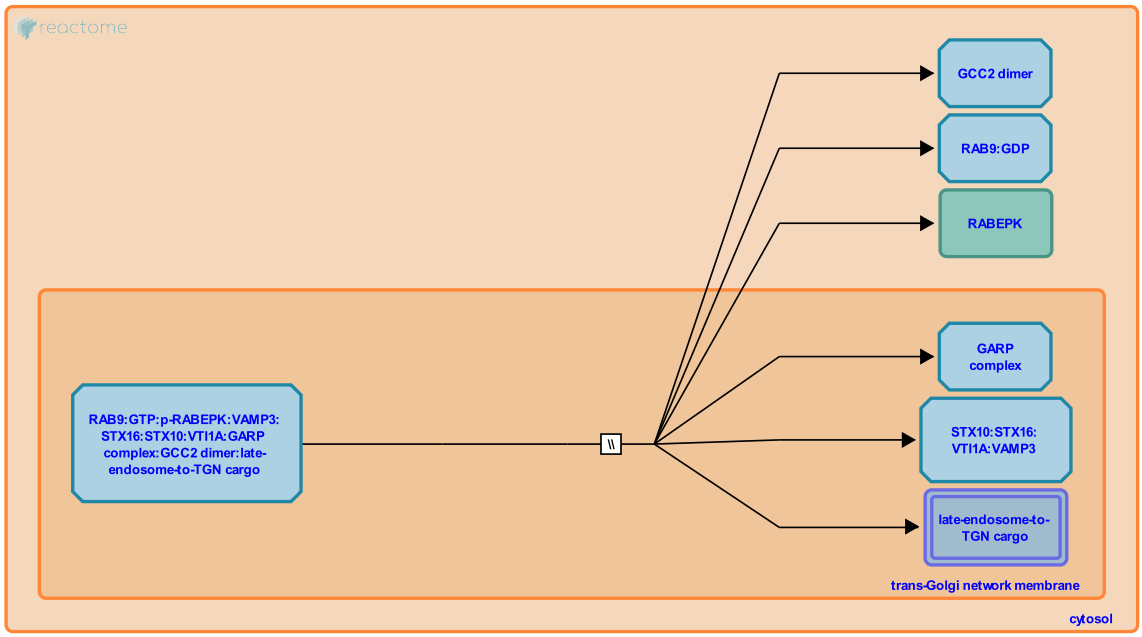
Fusion of late-endosome derived vesicles at the TGN ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814671

Type: omitted

Compartments: trans-Golgi network membrane



After capture at the trans-Golgi network by SNAREs and tethering factors, late endosome-derived vesicles undergo membrane fusion, delivering cargo and the cis-SNARE complex to the TGN membrane. The details of this fusion event are not fully established (reviewed in Pfeffer, 2011).

Preceded by: Tethering of late endosome-derived vesicles by GARP, STX10:ST16:VTI1A and Golgins

Followed by: SNAPs and NSF hexamer bind cis-SNARE at the TGN

Literature references

Pfeffer, SR. (2011). Entry at the trans-face of the Golgi. *Cold Spring Harb Perspect Biol, 3.* ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

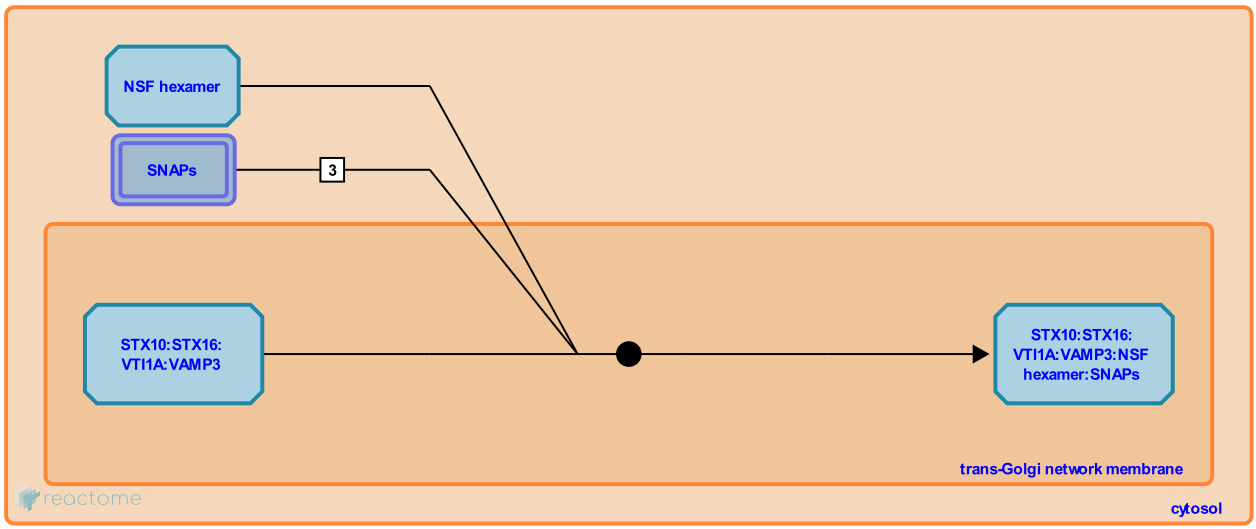
SNAPs and NSF hexamer bind cis-SNARE at the TGN ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814676

Type: binding

Compartments: trans-Golgi network membrane



After membrane fusion, the 4-membered cis-SNARE complex is dissociated in an ATP-dependent manner by SNAP and NSF (Mayer et al, 1996; Sollner et al, 1993; reviewed in Jahn and Scheller, 2006; Sudhof and Rothman, 2009).

Preceded by: Fusion of late-endosome derived vesicles at the TGN

Followed by: ATP hydrolysis by NSF disassembles the cis-SNARE at the TGN

Literature references

Haas, A., Mayer, A., Wickner, W. (1996). Sec18p (NSF)-driven release of Sec17p (alpha-SNAP) can precede docking and fusion of yeast vacuoles. *Cell, 85*, 83-94. ↗

Söllner, T., Whiteheart, SW., Scheller, RH., Bennett, MK., Rothman, JE. (1993). A protein assembly-disassembly pathway in vitro that may correspond to sequential steps of synaptic vesicle docking, activation, and fusion. *Cell, 75*, 409-18. ↗

Südhof, TC., Rothman, JE. (2009). Membrane fusion: grappling with SNARE and SM proteins. *Science, 323*, 474-7. ↗

Scheller, RH., Jahn, R. (2006). SNAREs--engines for membrane fusion. *Nat. Rev. Mol. Cell Biol., 7*, 631-43. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

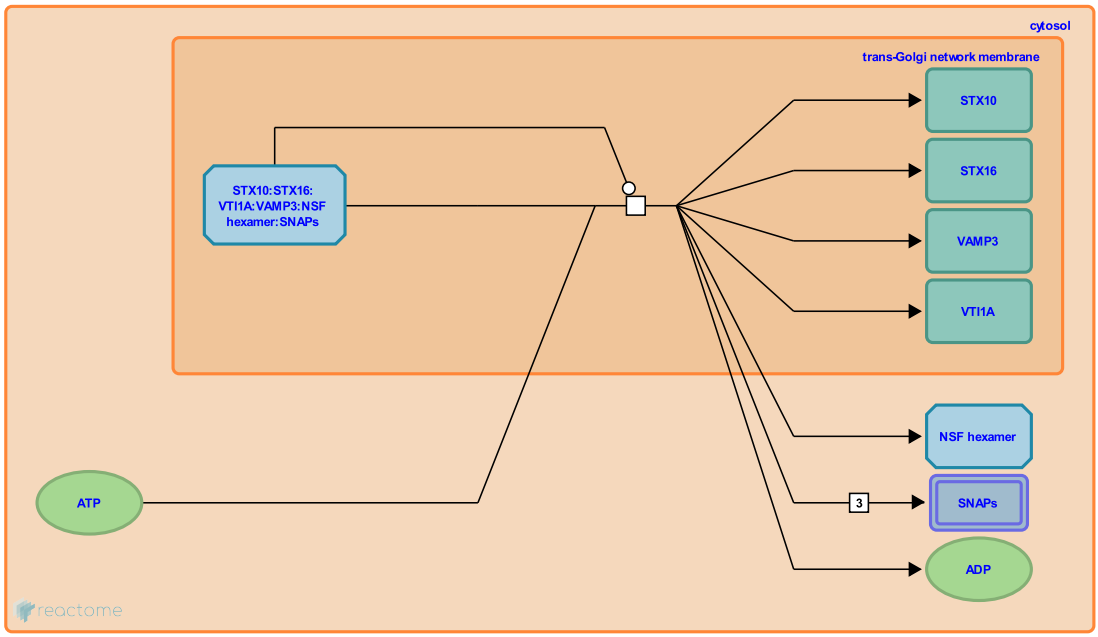
ATP hydrolysis by NSF disassembles the cis-SNARE at the TGN ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-6814678

Type: transition

Compartments: trans-Golgi network membrane



NSF-dependent hydrolysis of ATP is required to disassociate the cis-SNARE complex, releasing the SNAREs for further rounds of membrane fusion (Mayer et al, 1996; Muller et al, 1999; Muller et al, 2002; Otto et al, 1997; Whiteheart et al, 2004; Yu et al, 1999; Zhao et al, 2012; Shah et al, 2015; reviewed in Sudhof and Rothman, 2009).

Preceded by: SNAPs and NSF hexamer bind cis-SNARE at the TGN

Literature references

Haas, A., Mayer, A., Wickner, W. (1996). Sec18p (NSF)-driven release of Sec17p (alpha-SNAP) can precede docking and fusion of yeast vacuoles. *Cell, 85*, 83-94. ↗

Hanson, PI., Jahn, R., Otto, H. (1997). Assembly and disassembly of a ternary complex of synaptobrevin, syntaxin, and SNAP-25 in the membrane of synaptic vesicles. *Proc. Natl. Acad. Sci. U.S.A., 94*, 6197-201. ↗

Yu, RC., Jahn, R., Brunger, AT. (1999). NSF N-terminal domain crystal structure: models of NSF function. *Mol. Cell, 4*, 97-107. ↗

Matveeva, EA., Whiteheart, SW. (2004). Multiple binding proteins suggest diverse functions for the N-ethylmaleimide sensitive factor. *J. Struct. Biol., 146*, 32-43. ↗

Südhof, TC., Rothman, JE. (2009). Membrane fusion: grappling with SNARE and SM proteins. *Science, 323*, 474-7. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

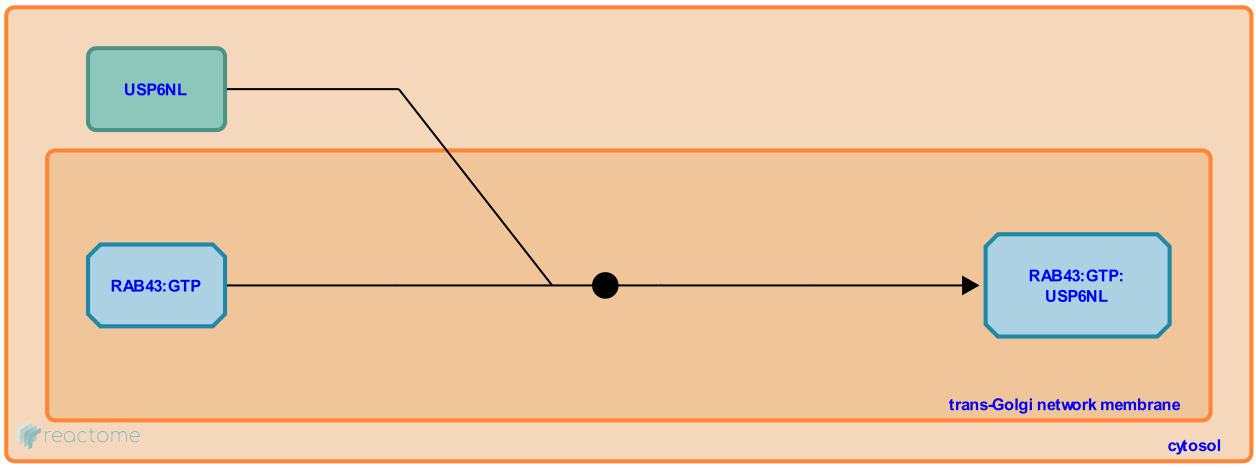
RAB43:GTP binds USP8NL ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-8847537

Type: binding

Compartments: trans-Golgi network membrane



RAB43 contributes to the maintenance of Golgi structure and is required for the RAB6-dependent retrograde trafficking of Shiga toxin (Fuchs et al, 2007; Haas et al, 2007). RAB43 appears to be localized to the cis side of the Golgi, so the details of how and when it affects Shiga transport remain to be clarified (Dejgaard et al, 2007). Screens of human cells identified USP6NL as a RAB43-specific GTPase activating (GAP) protein that is also implicated in Shiga trafficking (Fuchs et al, 2007; Haas et al, 2007; reviewed in Pfeffer, 2011).

Followed by: RAB43 hydrolyses GTP

Literature references

Spooner, RA., Barr, FA., Lord, JM., Haas, AK., Yoshimura, S., Fuchs, E. (2007). Specific Rab GTPase-activating proteins define the Shiga toxin and epidermal growth factor uptake pathways. *J. Cell Biol., 177*, 1133-43. ↗

Presley, JF., Verbich, D., Lodge, R., Murshid, A., Dejgaard, K., Kizilay, O. et al. (2008). Rab18 and Rab43 have key roles in ER-Golgi trafficking. *J. Cell. Sci., 121*, 2768-81. ↗

Pfeffer, SR. (2011). Entry at the trans-face of the Golgi. *Cold Spring Harb Perspect Biol, 3*. ↗

Barr, FA., Haas, AK., Stephens, DJ., Yoshimura, S., Fuchs, E., Preisinger, C. (2007). Analysis of GTPase-activating proteins: Rab1 and Rab43 are key Rabs required to maintain a functional Golgi complex in human cells. *J. Cell. Sci., 120*, 2997-3010. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

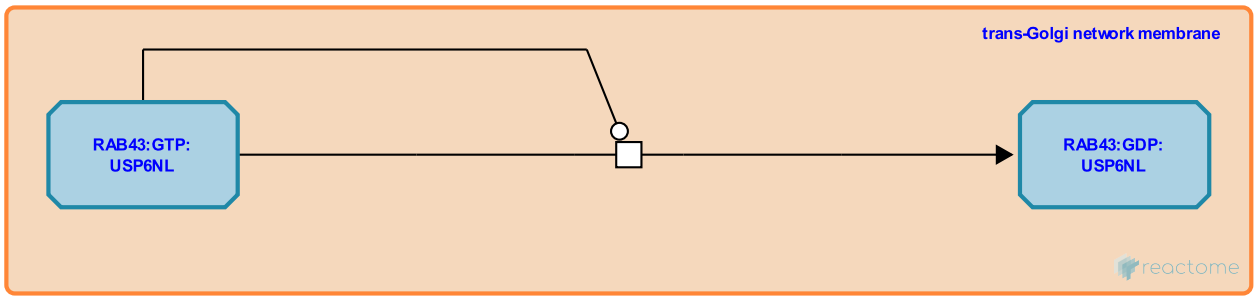
RAB43 hydrolyses GTP ↗

Location: Retrograde transport at the Trans-Golgi-Network

Stable identifier: R-HSA-8847534

Type: transition

Compartments: trans-Golgi network membrane



RAB GAP USP6NL stimulates the GTPase activity of RAB43, promoting hydrolysis of GTP. Both RAB43 and USP6NL have been identifed as contributing to the retrograde transport of Shiga toxin to the Golgi, however the details of their roles remain to be elucidated (Fuchs et al, 2007; Haas et al, 2007; reviewed in Pfeffer, 2011).

Preceded by: RAB43:GTP binds USP8NL

Literature references

Spooner, RA., Barr, FA., Lord, JM., Haas, AK., Yoshimura, S., Fuchs, E. (2007). Specific Rab GTPase-activating proteins define the Shiga toxin and epidermal growth factor uptake pathways. *J. Cell Biol., 177*, 1133-43. ↗

Pfeffer, SR. (2011). Entry at the trans-face of the Golgi. *Cold Spring Harb Perspect Biol, 3*. ↗

Barr, FA., Haas, AK., Stephens, DJ., Yoshimura, S., Fuchs, E., Preisinger, C. (2007). Analysis of GTPase-activating proteins: Rab1 and Rab43 are key Rabs required to maintain a functional Golgi complex in human cells. *J. Cell. Sci., 120*, 2997-3010. ↗

Editions

2015-11-09	Authored, Edited	Rothfels, K.
2016-02-02	Reviewed	Gillespie, ME.

Table of Contents