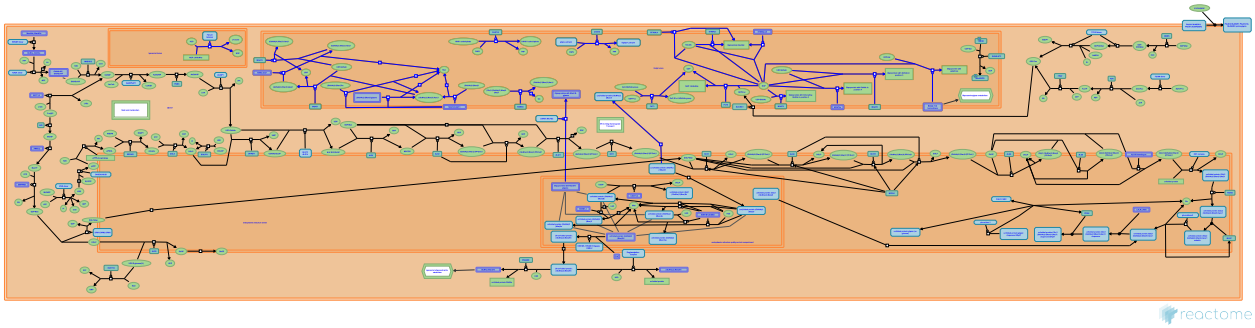
Transport to the Golgi and subsequent modification



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17/05/2024

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. ↗

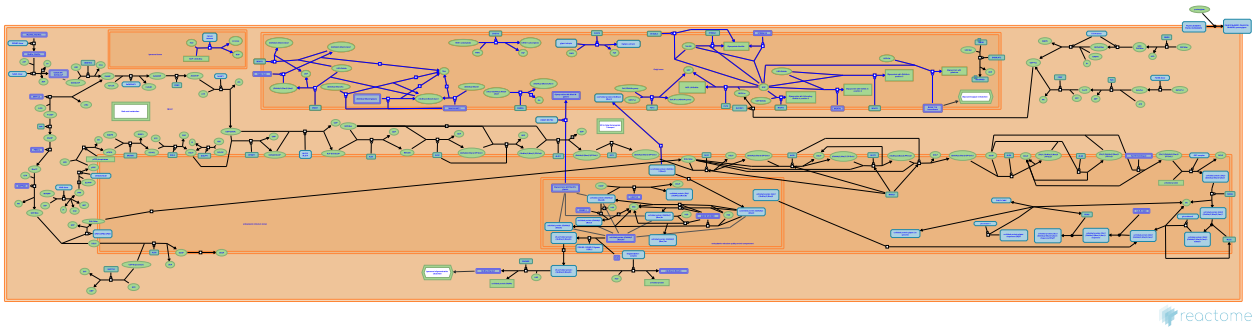
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Transport to the Golgi and subsequent modification ↗

Stable identifier: R-HSA-948021



At least two mechanisms of transport of proteins from the ER to the Golgi have been described. One is a general flow requiring no export signals (Wieland et al, 1987; Martinez-Menarguez et al, 1999). The other is mediated by LMAN1/MCFD2, mannose-binding lectins that recognize a glycan signal (Zhang B et al, 2003).

Literature references

Slot, JW., Klumperman, J., Martinez-Menárguez, JA., Geuze, HJ. (1999). Vesicular tubular clusters between the ER and Golgi mediate concentration of soluble secretory proteins by exclusion from COPI-coated vesicles. *Cell, 98*, 81-90. ↗

Serafini, TA., Wieland, FT., Rothman, JE., Gleason, ML. (1987). The rate of bulk flow from the endoplasmic reticulum to the cell surface. *Cell, 50*, 289-300. ↗

Ruiz-Saez, A., Cunningham, MA., Pipe, SW., Kaufman, RJ., McVey, JH., Nichols, WC. et al. (2003). Bleeding due to disruption of a cargo-specific ER-to-Golgi transport complex. *Nat Genet, 34*, 220-5. ↗

Editions

2009-11-10	Authored	Dall'Olio, GM.
2010-09-15	Edited	Jassal, B.
2010-11-18	Reviewed	Gagneux, P.

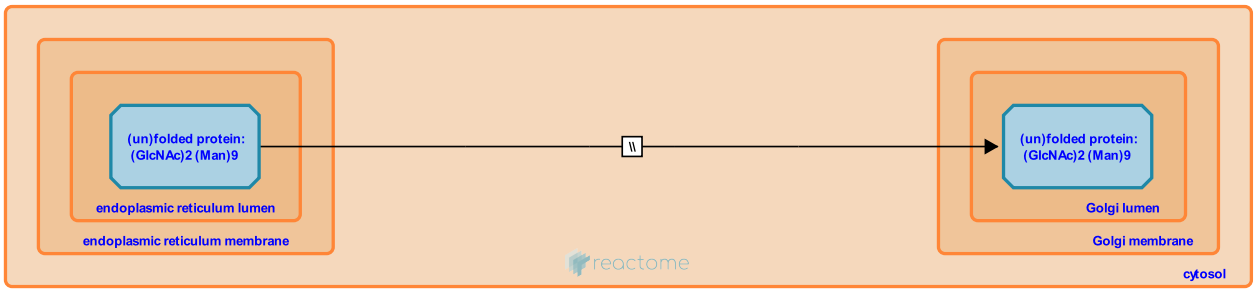
Correctly folded glycoproteins translocate to the Golgi ↗

Location: Transport to the Golgi and subsequent modification

Stable identifier: R-HSA-915148

Type: omitted

Compartments: cytosol



Correctly folded proteins, after being released from the Calnexin/Calreticulin cycle, are translocated to the Golgi (Hauri H et al, 2000; Hauri HP et al, 2002; Molinari, 2007).

Literature references

Molinari, M. (2007). N-glycan structure dictates extension of protein folding or onset of disposal. *Nat Chem Biol, 3*, 313-20. ↗

Liang, L., Nufer, O., Hauri, HP., Tekaya, HB., Breuza, L. (2002). Lectins and protein traffic early in the secretory pathway. *Biochem Soc Symp*, 73-82. ↗

Nufer, O., Hauri, H., Kuhn, F., Appenzeller, C. (2000). Lectins and traffic in the secretory pathway. *FEBS Lett, 476*, 32-7. ↗

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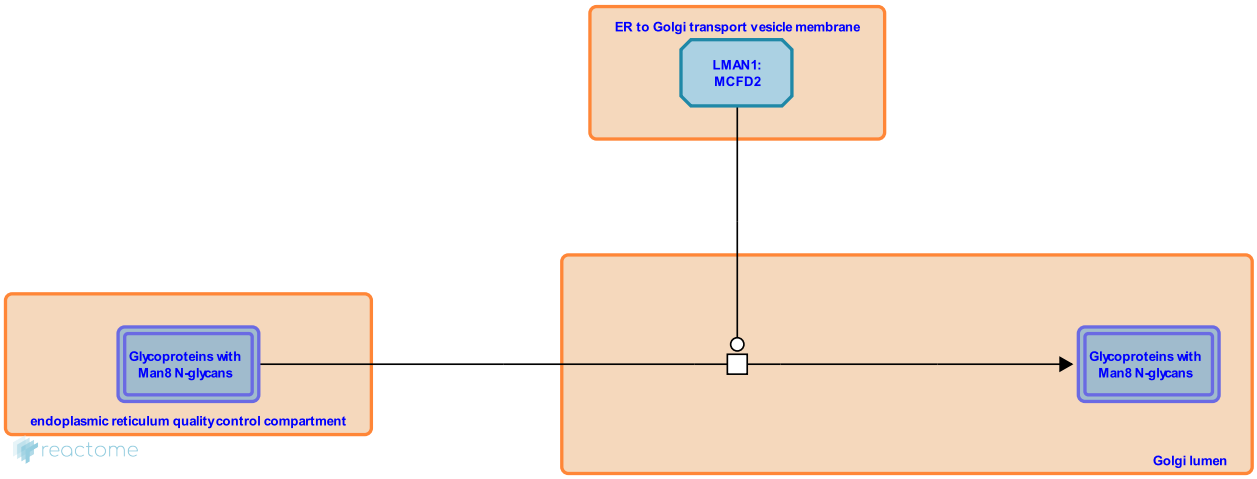
Transport of glycoproteins with Man8 (or Man9) N-glycans to the Golgi ↗

Location: Transport to the Golgi and subsequent modification

Stable identifier: R-HSA-947991

Type: transition

Compartments: Golgi lumen, endoplasmic reticulum quality control compartment



The LMAN1(also known as ERGIC-53)/MCFD2 complex recognizes Man8 and Man9 N-glycans released by the Calnexin/Calreticulin cycle and mediate their transport to the Golgi (Nyefeler B et al, 2003; Zhang B et al, 2003). Man8 glycan transfer is shown here.

Literature references

Hauri, HP., Mori, K., Nufer, O., Matsui, T., Nyfeler, B. (2003). The cargo receptor ERGIC-53 is a target of the unfolded protein response. *Biochem Biophys Res Commun, 304*, 599-604. ↗

Ruiz-Saez, A., Cunningham, MA., Pipe, SW., Kaufman, RJ., McVey, JH., Nichols, WC. et al. (2003). Bleeding due to disruption of a cargo-specific ER-to-Golgi transport complex. *Nat Genet, 34*, 220-5. ↗

Editions

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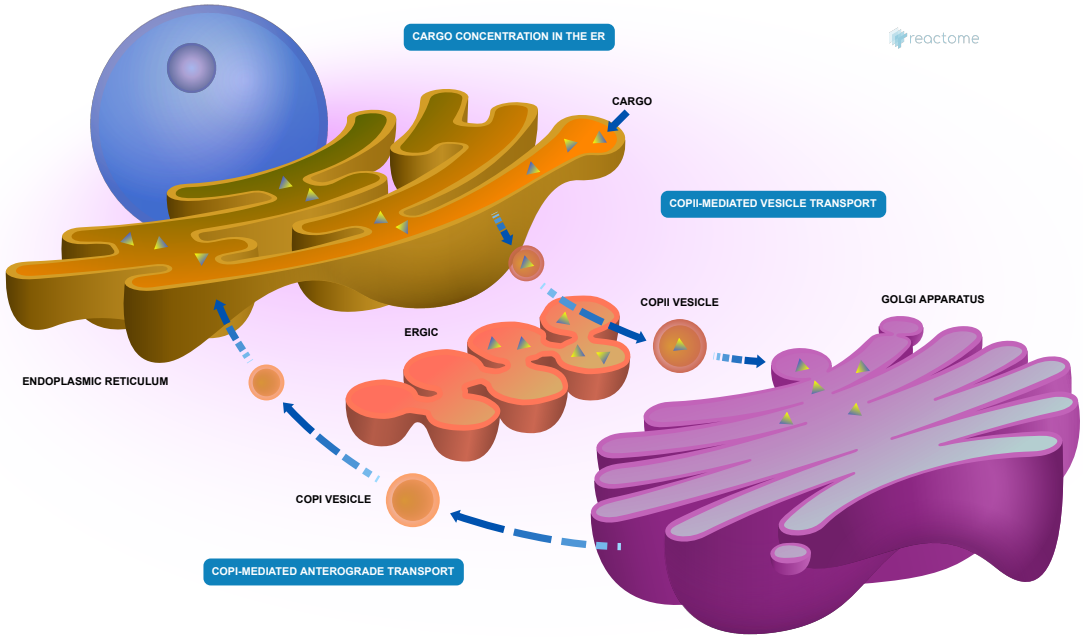
ER to Golgi Anterograde Transport ↗

Location: Transport to the Golgi and subsequent modification

Stable identifier: R-HSA-199977



Secretory cargo destined to be secreted or to arrive at the plasma membrane (PM) leaves the ER via distinct exit sites. This cargo is destined for the Golgi apparatus for further processing. About 25% of the proteome may be exported from the ER in human cells. This cargo is recognized and concentrated into COPII vesicles, which range in size from 60-90 nm, and move cargo from the ER to the ERGIC. Soluble cargo in the ER lumen is concentrated into COPII vesicles through interaction with a receptor with the receptor subsequently recycled to the ER in COPI vesicles through retrograde traffic. The ERGIC (ER-to-Golgi intermediate compartment, also known as vesicular-tubular clusters, VTCs) is a stable, biochemically distinct compartment located adjacent to ER exit sites. Retrograde traffic makes use of microtubule-directed COPI-coated vesicles, carrying ER proteins and membrane back to the ER.

Literature references

Kirchhausen, Tomas. (2000). Three ways to make a vesicle. *Nat Rev Mol Cell Biol, 1*, 187-98. ↗

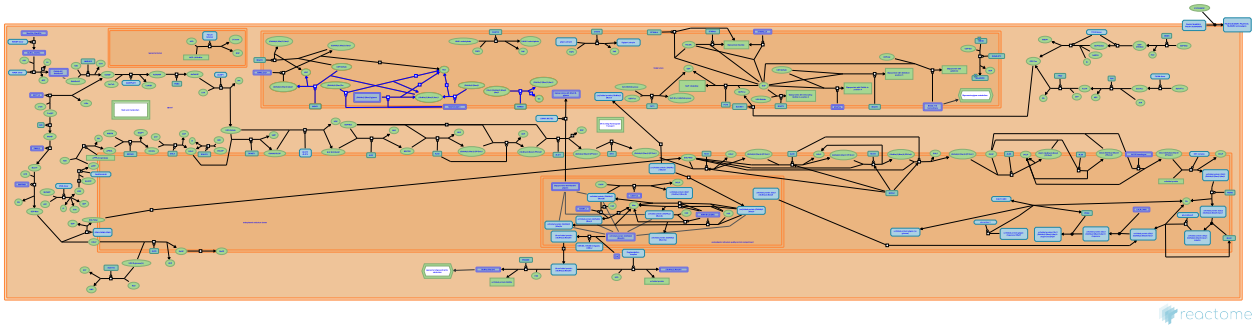
Editions

2007-07-14	Authored	Gillespie, ME.
2007-07-19	Edited	Gillespie, ME.
2010-11-18	Reviewed	Gagneux, P.
2015-04-18	Revised	Rothfels, K.
2015-08-18	Revised	Gillespie, ME.

N-glycan trimming and elongation in the cis-Golgi ↗

Location: Transport to the Golgi and subsequent modification

Stable identifier: R-HSA-964739



After the transport of the glycoprotein to the cis-Golgi, the pathway of N-glycosylation bifurcates. Some N-glycans can be moved to subsequent steps of the secretory pathway without further modifications, or alternatively, with the removal of a few mannoses (Oligo Mannoses pathway). In yeast and other unicellular species, a series of mannose residues are added (High Mannoses pathway). The presence of this modification is a major obstacle to the production of pharmaceutical drugs in yeast, where the HighMannose pathway must be inhibited or modified in order to avoid the presence of high mannose xenoglycans.
The first N-glycan modification step is the trimming of up to four mannoses by one of three mannosidase enzymes. Moreover, Glycoproteins that have not entered in the Calnexin/Calreticulin cycle or that have not had their glucose residues trimmed earlier in the ER, can enter the main pathway here due to the existence to an alternative route catalyzed by the enzyme Endomannosidase I (Schachter, 2000; Stanley et al, 2009)

Literature references

Esko, JD., Varki, A., Bertozzi, CR., Schachter, H., Etzler, ME., Freeze, HH. et al. (2009). N-Glycans.

Schachter, H. (2000). The joys of HexNAc. The synthesis and function of N- and O-glycan branches. *Glycoconj J, 17*, 465-83. ↗

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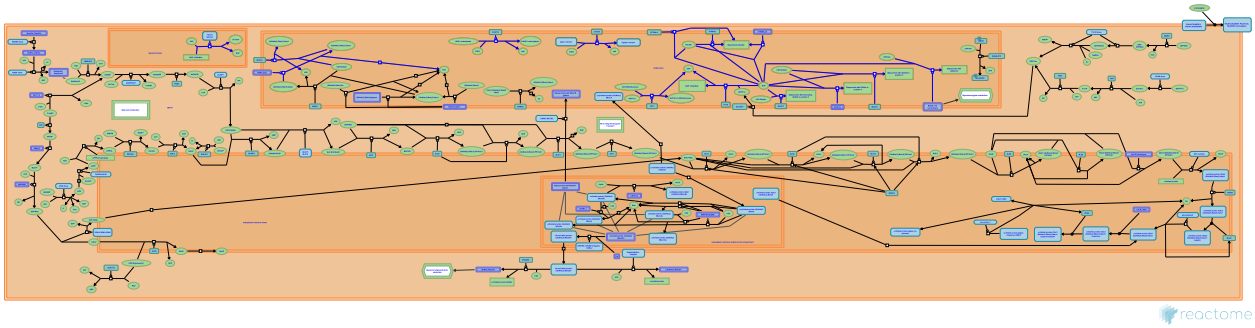
N-glycan antennae elongation in the medial/trans-Golgi ↗

Location: Transport to the Golgi and subsequent modification

Stable identifier: R-HSA-975576



In the latter compartments of the distal Golgi the N-Glycan is further modified, leading to the wide range of N-Glycans observed in multicellular organisms. The first step of N-Glycan elongation in the Golgi is the addition of a GlcNAc residue on the alpha 1,3 branch by the enzyme MGAT1 (GlcNAc-TI), which commits the elongation pathway to Complex or Hybrid N-Glycans from Oligomannose N-Glycans. At this point, the pathway bifurcates again to generate Complex or Hybrid N-Glycans. The addition of a GlcNAc in the middle of the two arms of the N-Glycan, catalyzed by MGAT3 (GNT-III), inhibits the removal of the mannoses on the alpha1,3 branches by MAN2 and the addition of a GlcNAc by MGAT2 (GlcNAc-TII), and commits the pathway toward the synthesis of hybrid N-Glycans. Alternatively, the removal of these mannoses and the action of MGAT2 leads to the synthesis of complex N-Glycans (Kornfeld and Kornfeld 1985).
The exact structure of the network of reactions leading to Complex or Hybrid N-Glycans is still not completely described and validated experimentally. Here we will annotate only one generic reaction for each of the enzymes known to participate in this process. For a better annotation on the reactions and genes involved in the synthesis of Complex and Hybrid N-Glycans we recommend the GlycoGene Database (Ito H. et al, 2010) (http://riodb.ibase.aist.go.jp/rcmg/ggdb/textsearch.jsp) for annotations on genes, and the Consortium for Functional Genomics (http://riodb.ibase.aist.go.jp/rcmg/ggdb/textsearch.jsp) for annotation of Glycan structures and reactions. Moreover, a computationally inferred prediction on the structure of this network is available through the software GlycoVis (Hossler P. et. al. 2006).

Literature references

Kornfeld, S., Kornfeld, R. (1985). Assembly of asparagine-linked oligosaccharides. *Annu Rev Biochem, 54*, 631-64. ↗

Hu, WS., Lee, MM., Hossler, P., Goh, LT. (2006). GlycoVis: visualizing glycan distribution in the protein N-glycosylation pathway in mammalian cells. *Biotechnol Bioeng, 95*, 946-60. ↗

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Ito, H., Narimatsu, H., Sato, T., Kameyama, A., Chiba, Y. (2010). In vitro and in vivo enzymatic syntheses and mass spectrometric database for N-glycans and o-glycans. *Methods Enzymol, 478*, 127-49. ↗

Editions

2009-11-10	Authored	Dall'Olio, GM.
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