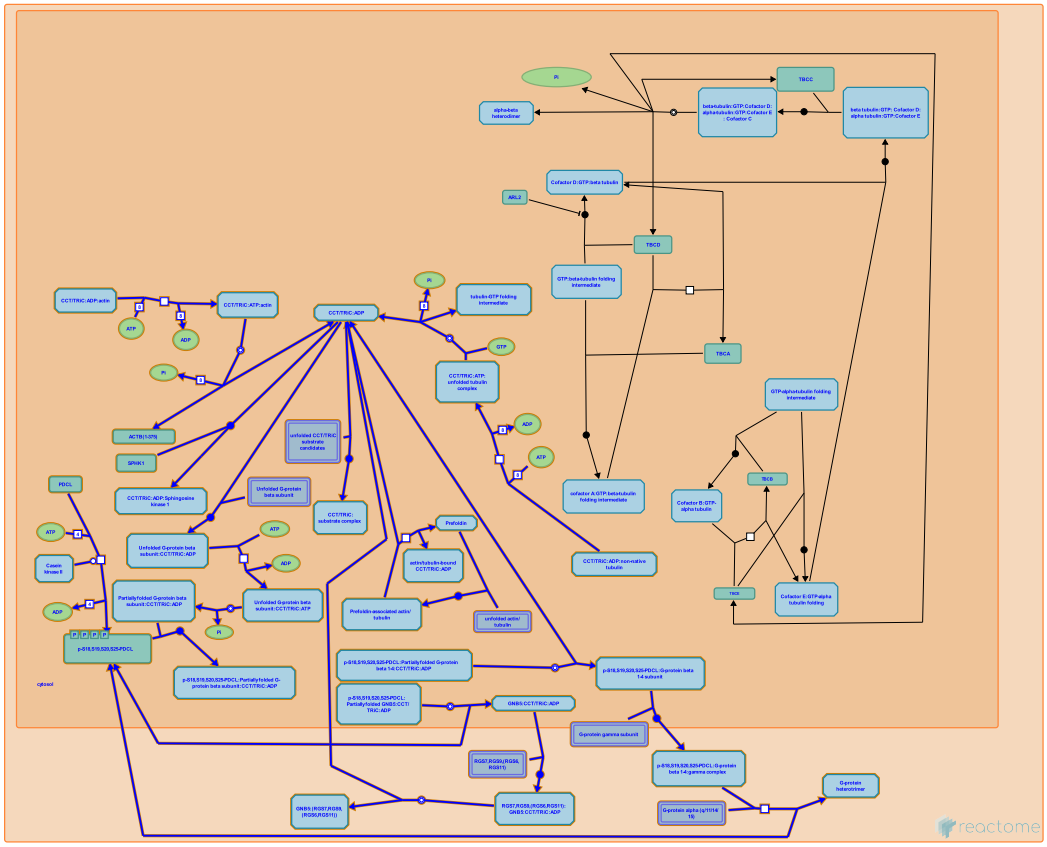
Chaperonin-mediated protein folding



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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.

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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.
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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. ↗

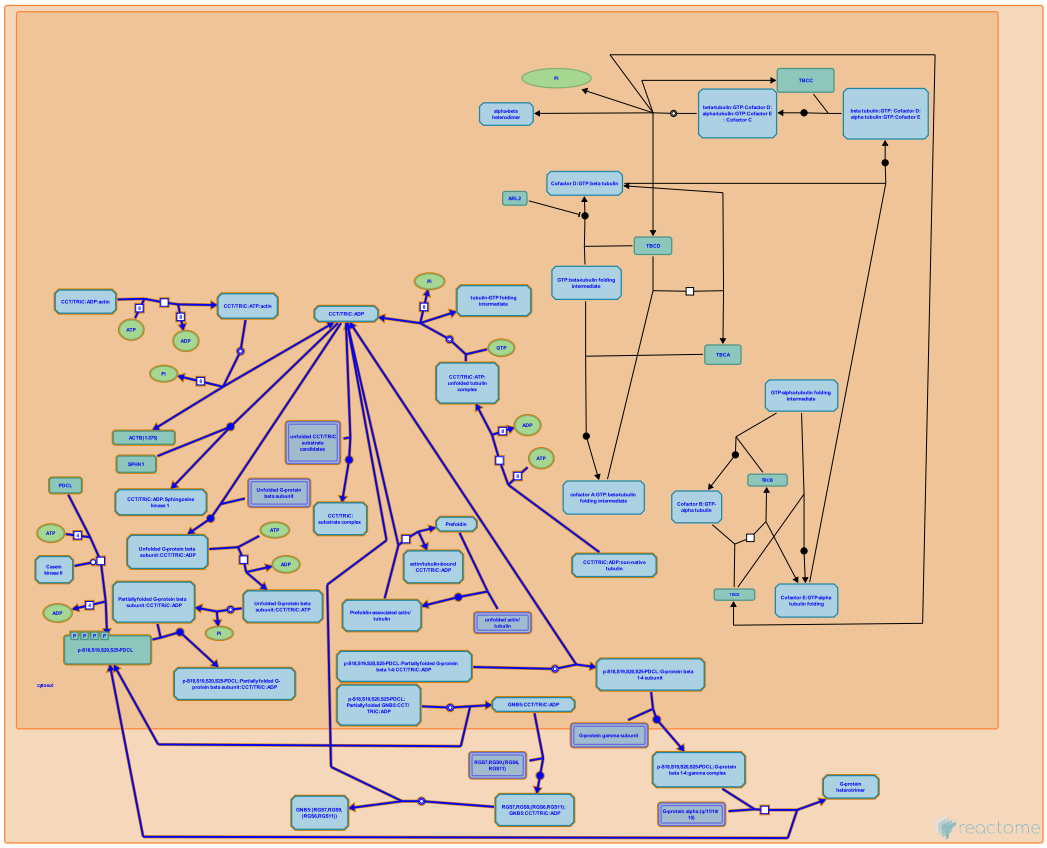
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Chaperonin-mediated protein folding ↗

Stable identifier: R-HSA-390466

Compartments: cytosol



The eukaryotic chaperonin TCP-1 ring complex (TRiC/ CCT) plays an essential role in the folding of a subset of proteins prominent among which are the actins and tubulins (reviewed in Altschuler and Willison, 2008). CCT/TRiC is an example of a type II chaperonin, defined (in contrast to type I) as functioning in the absence of a cochaperonin. TriC/CCT is a multisubunit toroidal complex that forms a cylinder containing two back-to-back stacked rings enclosing a cavity where substrate folding occurs in an ATP dependent process (reviewed in Altschuler and Willison, 2008). CCT/TriC contains eight paralogous subunits that are conserved throughout eukaryotic organisms (Leroux and Hartl 2000; Archibald et al. 2001; Valpuesta et al. 2002). CCT-mediated folding of non-native substrate protein involves capture through hydrophobic contacts with multiple chaperonin subunits followed by transfer of the protein into the central ring cavity where it folds. Although folding is initiated within this central cavity, only 5%-20% of proteins that are released have partitioned to the native state. The remaining portion is then recaptured by other chaperonin molecules (Cowan and Lewis 2001). This cycling process may be repeated multiple times before a target protein partitions to the native state. In the cell, binding to CCT occurs via presentation of target protein bound to upstream chaperones. During translation, the emerging polypeptide chain may be transferred from the ribosome to CCT via the chaperone Prefoldin (Vainberg et al., 1998) or the Hsp70 chaperone machinery (Melville et al., 2003). While the majority of CCT substrates ultimately partition to the native state as soluble, monomeric proteins, alpha and beta tubulin are unusual in that they require additional cofactors that are required to assemble the tubulin heterodimer (Cowan and Lewis 2001).

Literature references

Lewis, SA., Cowan, NJ. (2001). Type II chaperonins, prefoldin, and the tubulin-specific chaperones. *Adv Protein Chem , 59*, 73-104. ↗

Meyer, AS., Reissmann, S., Frydman, J., Spiess, C. (2004). Mechanism of the eukaryotic chaperonin: protein folding in the chamber of secrets. *Trends Cell Biol, 14*, 598-604. ↗

Editions

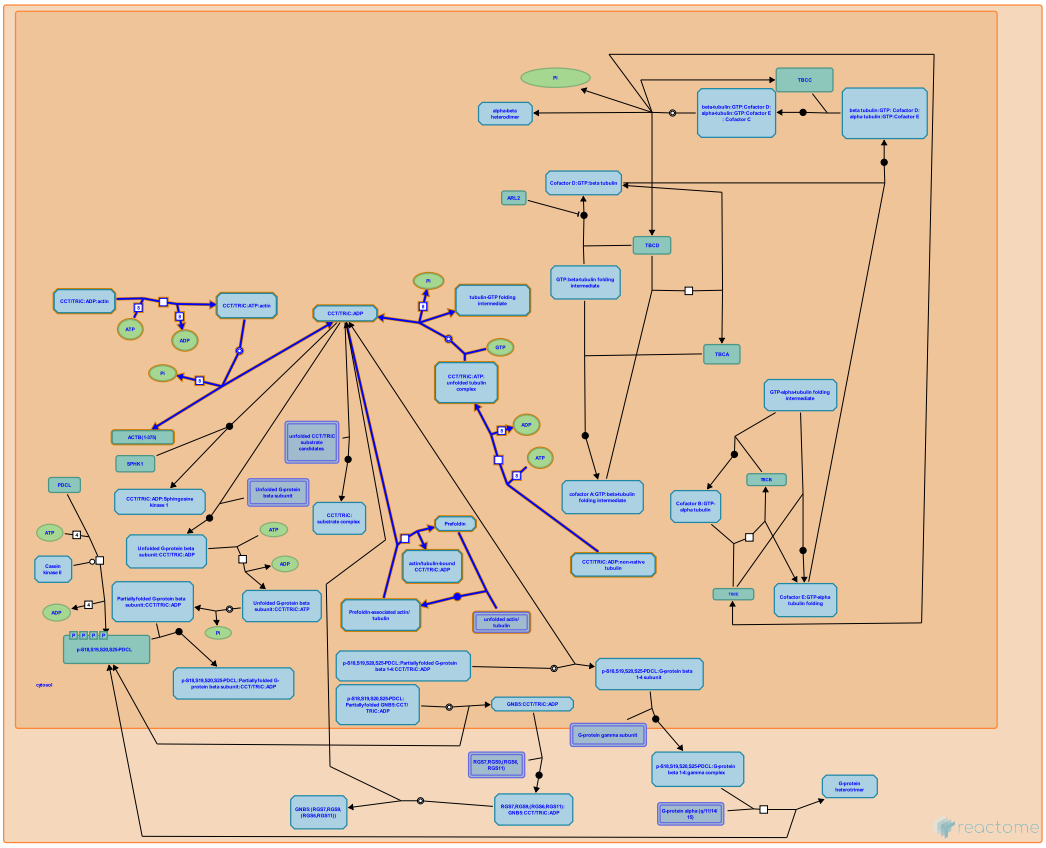
2008-12-01	Authored	Matthews, L.
2009-01-21	Reviewed	Cowan, NJ.
2009-02-21	Edited	Matthews, L.

Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding ↗

Location: Chaperonin-mediated protein folding

Stable identifier: R-HSA-389958

Compartments: cytosol



In the case of actin and tubulin folding, and perhaps other substrates, the emerging polypeptide chain is transferred from the ribosome to TRiC via Prefoldin (Vainberg et al., 1998).

Literature references

Klein, HL., Rommelaere, H., Vandekerckhove, J., Lewis, SA., Cowan, NJ., Ampe, C. et al. (1998). Prefoldin, a chaperone that delivers unfolded proteins to cytosolic chaperonin. *Cell, 93*, 863-73. ↗

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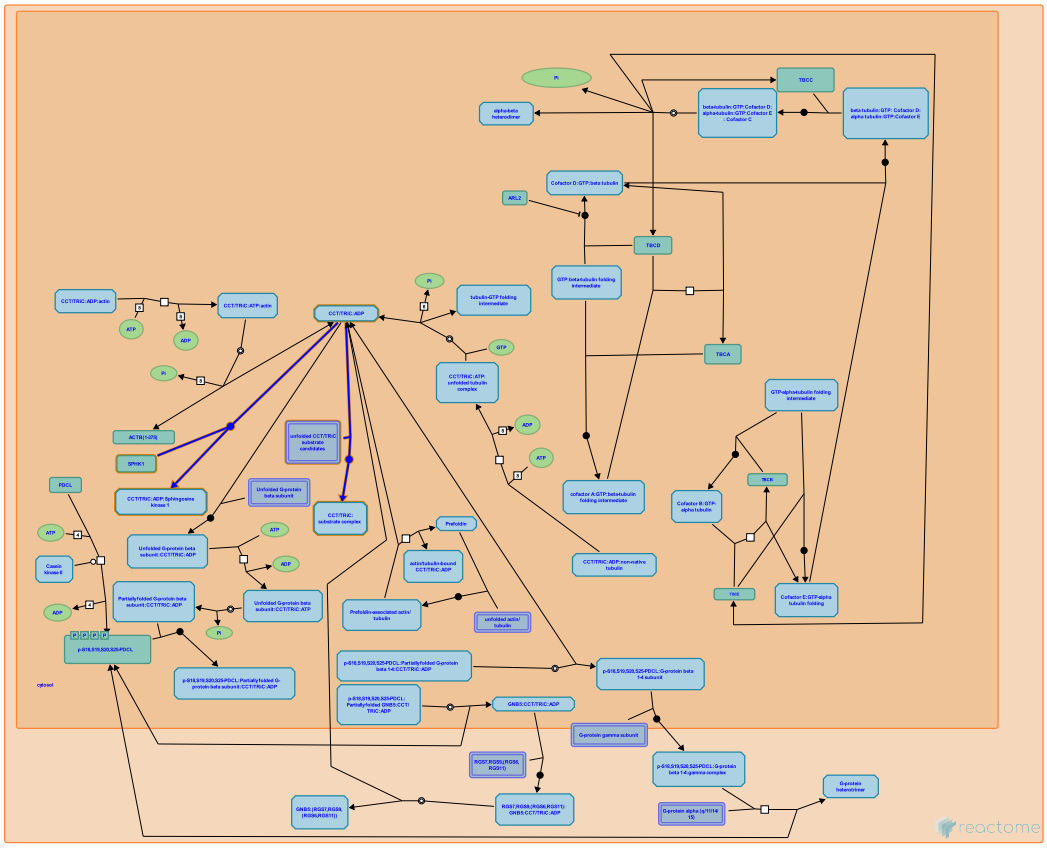
Association of TriC/CCT with target proteins during biosynthesis ↗

Location: Chaperonin-mediated protein folding

Stable identifier: R-HSA-390471

Compartments: cytosol



TRiC has broad recognition specificities, but in the cell it interacts with only a defined set of substrates (Yam et al. 2008). Many of its substrates that are targeted during biosynthesis are conserved between mammals and yeast (Yam et al. 2008).

Literature references

Lin, HT., Burlingame, A., Frydman, J., Xia, Y., Gerstein, M., Yam, AY. (2008). Defining the TRiC/CCT interactome links chaperonin function to stabilization of newly made proteins with complex topologies. *Nat Struct Mol Biol, 15*, 1255-62. ↗

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2008-12-01	Authored	Matthews, L.
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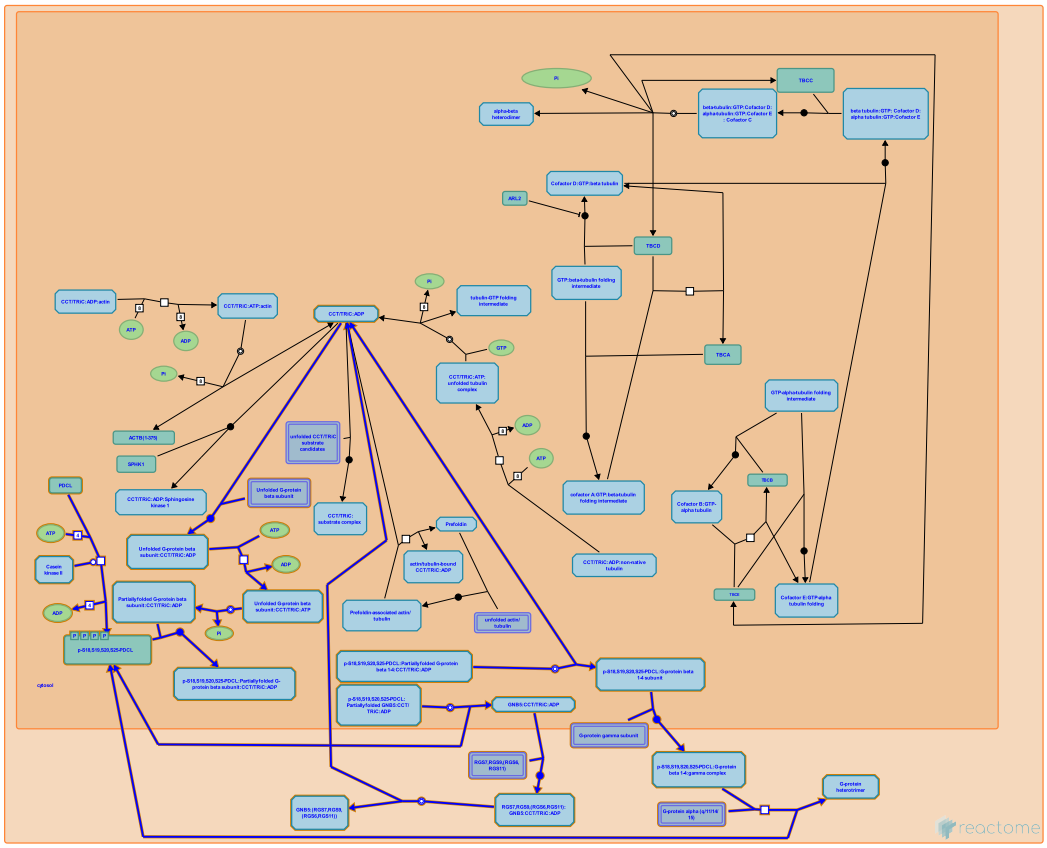
Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding ↗

Location: Chaperonin-mediated protein folding

Stable identifier: R-HSA-6814122



The chaperonin complex TRiC/CCT is needed for the proper folding of all five G-protein beta subunits (Wells et al. 2006). TRiC/CCT cooperates with the phosducin-like protein PDCL (commonly known as PhLP or PhLP1), which interacts with both TRiC/CCT and G-protein beta subunits 1-5 (GNB1, GNB2, GNB3, GNB4, GNB5) (Dupre et al. 2007, Howlett et al. 2009). PDCL enables completion of G-protein beta folding by TRiC/CCT, promotes release of folded G-protein beta subunits 1-4 (GNB1, GNB2, GNB3, GNB4) from the chaperonin complex, and facilitates the formation of the heterodimeric G-protein beta:gamma complex between G-protein beta subunits 1-4 and G-protein gamma subunits 1-12 (Lukov et al. 2005, Lukov et al. 2006, Howlett et al. 2009, Lai et al. 2013, Plimpton et al. 2015, Xie et al. 2015). In the case of G-protein beta 5 (GNB5), PDCL stabilizes the interaction of GNB5 with the TRiC/CCT and promotes GNB5 folding, thus positively affecting formation of GNB5 dimers with RGS family proteins (Howlett et al. 2009, Lai et al. 2013, Tracy et al. 2015). However, over-expression of PDCL interferes with formation of GNB5:RGS dimers as PDCL and RGS proteins bind to the same regions of the GNB5 protein (Howlett et al. 2009).

Literature references

Mamarbachi, AM., Dupré, DJ., Richer, M., Robitaille, M., Ethier, N., Hébert, TE. (2007). Dopamine receptor-interacting protein 78 acts as a molecular chaperone for Ggamma subunits before assembly with Gbeta. *J. Biol. Chem., 282*, 13703-15. ↗

Frederick, JM., Lai, CW., Chen, CK., Baehr, W., Kolesnikov, AV., Blake, DR. et al. (2013). Phosducin-like protein 1 is essential for G-protein assembly and signaling in retinal rod photoreceptors. *J. Neurosci., 33*, 7941-51. ↗

Dingus, J., Hildebrandt, JD., Wells, CA. (2006). Role of the chaperonin CCT/TRiC complex in G protein betagamma-dimer assembly. *J. Biol. Chem., 281*, 20221-32. ↗

Gray, AJ., Hunter, JM., Howlett, AC., Willardson, BM. (2009). Role of molecular chaperones in G protein beta5/regulator of G protein signaling dimer assembly and G protein betagamma dimer specificity. *J. Biol. Chem., 284*, 16386-99. ↗

Thulin, CD., Lukov, GL., Ludtke, PJ., Hu, T., Carter, MD., Baker, CM. et al. (2006). Mechanism of assembly of G protein betagamma subunits by protein kinase CK2-phosphorylated phosducin-like protein and the cytosolic chaperonin complex. *J. Biol. Chem., 281*, 22261-74. ↗

Editions

2015-11-30	Authored, Edited	Orlic-Milacic, M.
2015-12-22	Reviewed	Willardson, BM.

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