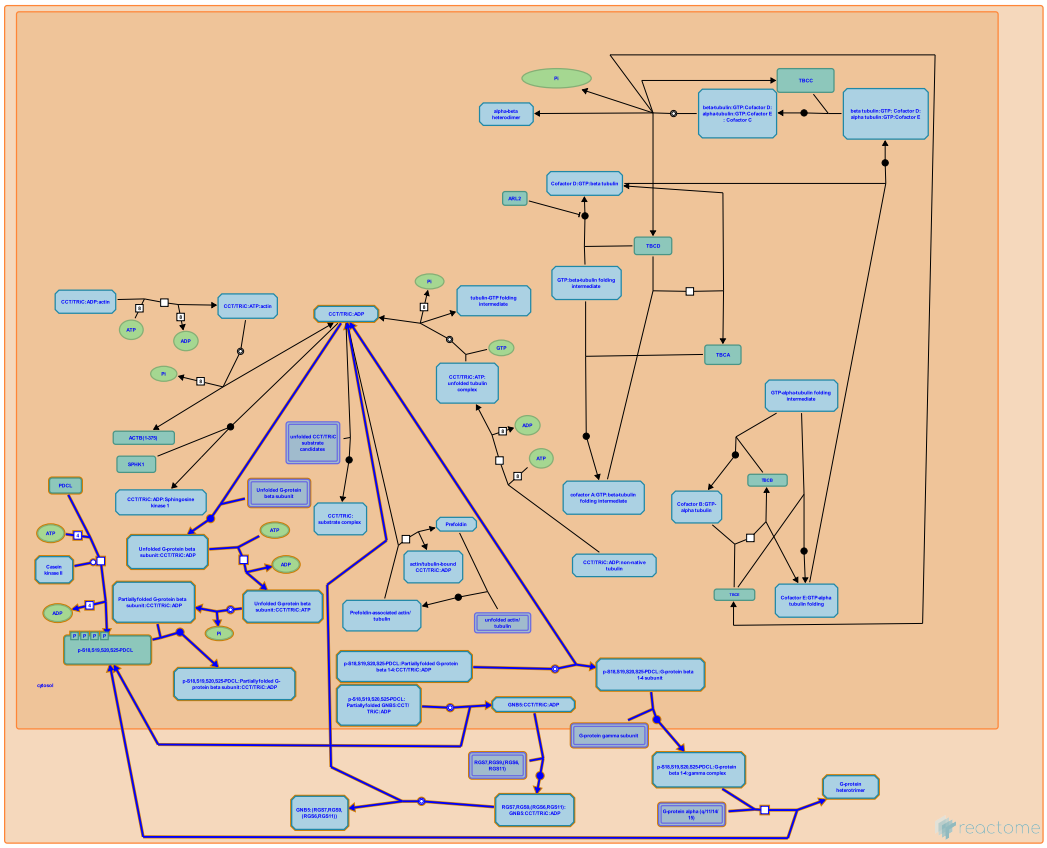
Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding



Orlic-Milacic, M., Willardson, BM.

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

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.

26/04/2024

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. ↗

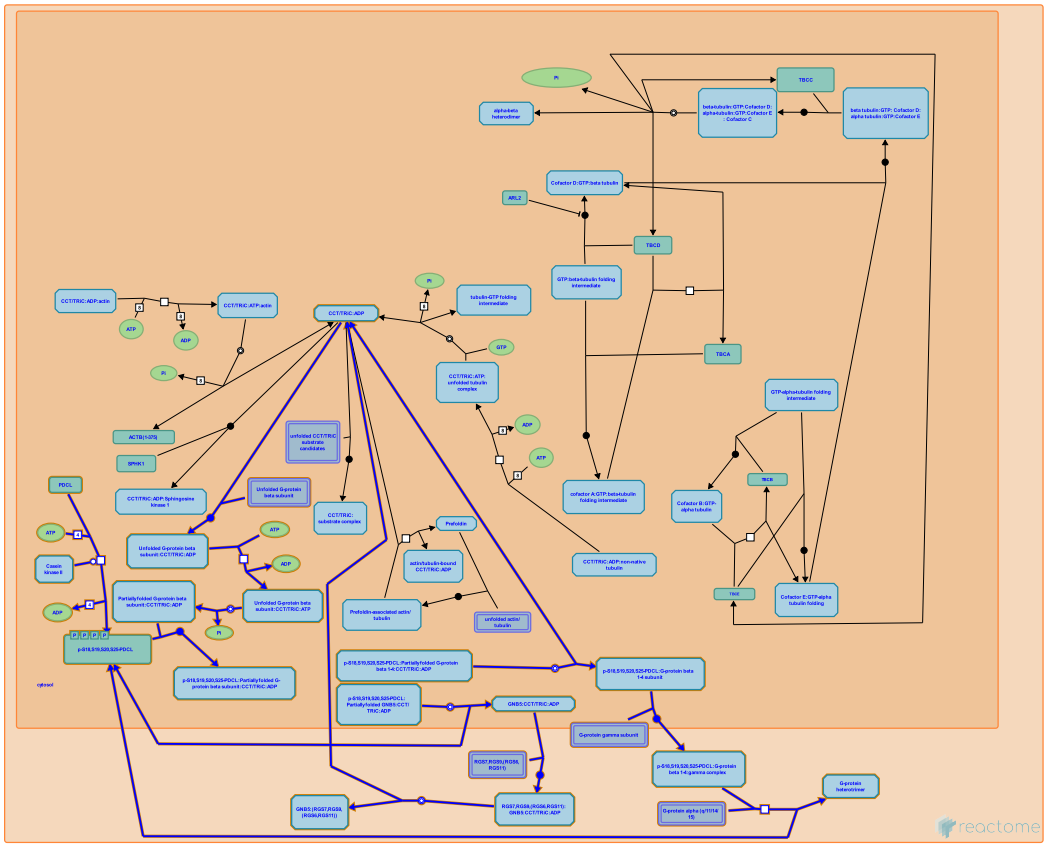
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta 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.

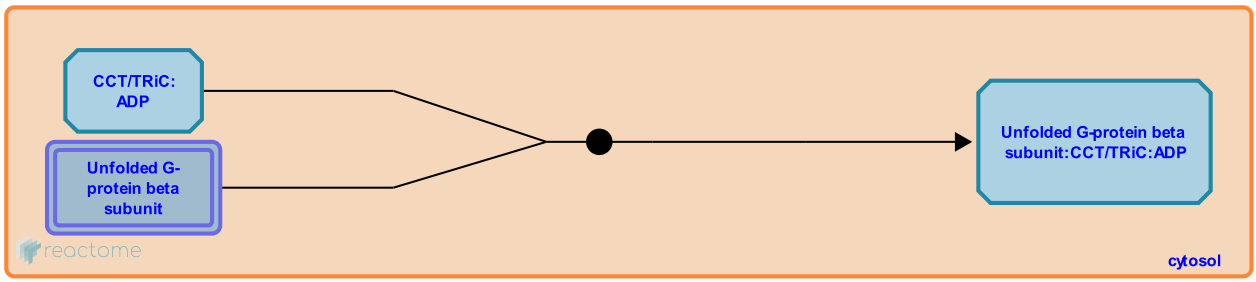
TRiC/CCT binds unfolded G-protein beta subunit ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-6814119

Type: binding

Compartments: cytosol



The TRiC/CCT chaperonin complex binds nascent, unfolded, G-protein beta subunit (GNB1, GNB2, GNB3, GNB4 or GNB5) (Wells et al. 2006). G-beta reaches a near-native state in the folding cavity of TRiC, except that TRiC cannot mediate the folding of the seven-bladed beta propeller of the G-protein beta to a stable conformation (Plimpton et al. 2015).

Followed by: ATP binds G-protein beta associated TRiC/CCT

Literature references

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. ↗

Makaju, A., Lai, CW., Prince, JT., Carrascosa, JL., Plimpton, RL., Cuellar, J. et al. (2015). Structures of the Gβ-CCT and PhLP1-Gβ-CCT complexes reveal a mechanism for G-protein β-subunit folding and Gβγ dimer assembly. *Proc. Natl. Acad. Sci. U.S.A., 112*, 2413-8. ↗

Editions

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

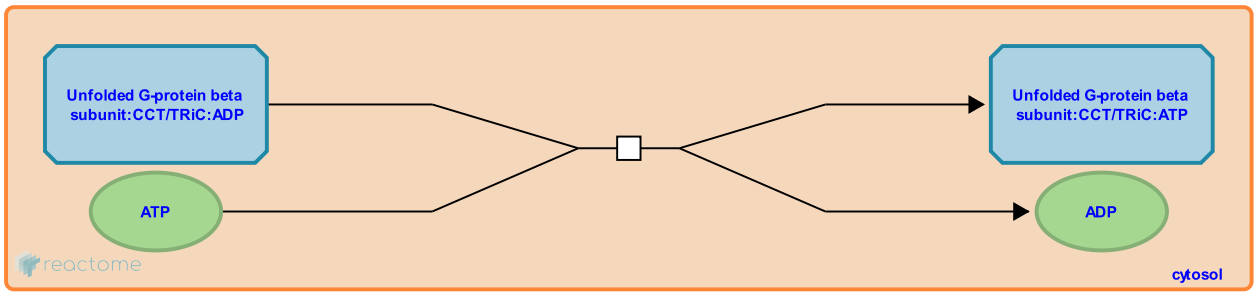
ATP binds G-protein beta associated TRiC/CCT ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-6814124

Type: transition

Compartments: cytosol



Based on structural studies of the TRiC/CCT chaperonin complex, the exchange of ADP for ATP enables conformational change of the chaperonin complex needed for folding of substrate proteins. It is assumed that TRiC/CCT-mediated folding of the G-protein beta subunit follows this universal pattern of TRiC/CCT functioning (Melki et al. 1997).

Preceded by: TRiC/CCT binds unfolded G-protein beta subunit

Followed by: ATP hydrolysis promotes folding of G-protein beta by TRiC/CCT

Literature references

Williams RC, Jr., Soulié, S., Melki, R., Batelier, G. (1997). Cytoplasmic chaperonin containing TCP-1: structural and functional characterization. *Biochemistry, 36*, 5817-26. ↗

Editions

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

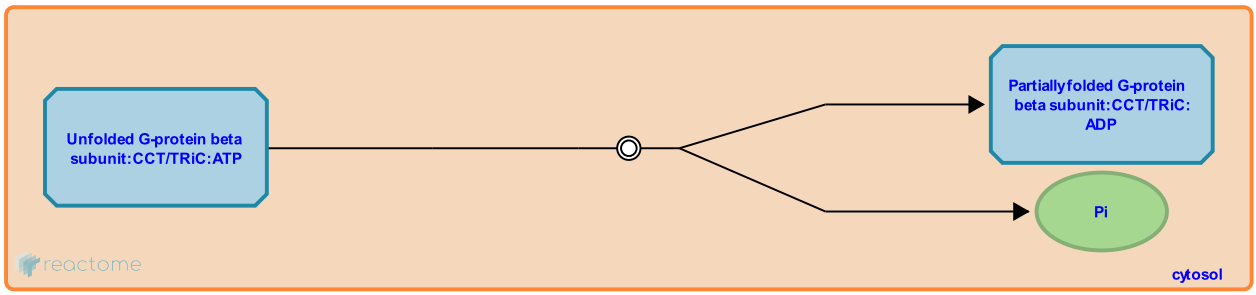
ATP hydrolysis promotes folding of G-protein beta by TRiC/CCT ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-6814120

Type: dissociation

Compartments: cytosol



In an ATP-dependent process, G-beta reaches a near-native state in the folding cavity of TRiC, except that TRiC cannot mediate the folding of the seven-bladed beta propeller of the G-protein beta to a stable conformation (Plimpton et al. 2015).

Preceded by: ATP binds G-protein beta associated TRiC/CCT

Followed by: PDCL binds G-protein beta and TRiC/CCT

Literature references

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. ↗

Lukov, GL., Hu, T., Hamm, HE., McLaughlin, JN., Willardson, BM. (2005). Phosducin-like protein acts as a molecular chaperone for G protein betagamma dimer assembly. *EMBO J., 24*, 1965-75. ↗

Makaju, A., Lai, CW., Prince, JT., Carrascosa, JL., Plimpton, RL., Cuellar, J. et al. (2015). Structures of the Gβ-CCT and PhLP1-Gβ-CCT complexes reveal a mechanism for G-protein β-subunit folding and Gβγ dimer assembly. *Proc. Natl. Acad. Sci. U.S.A., 112*, 2413-8. ↗

Editions

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

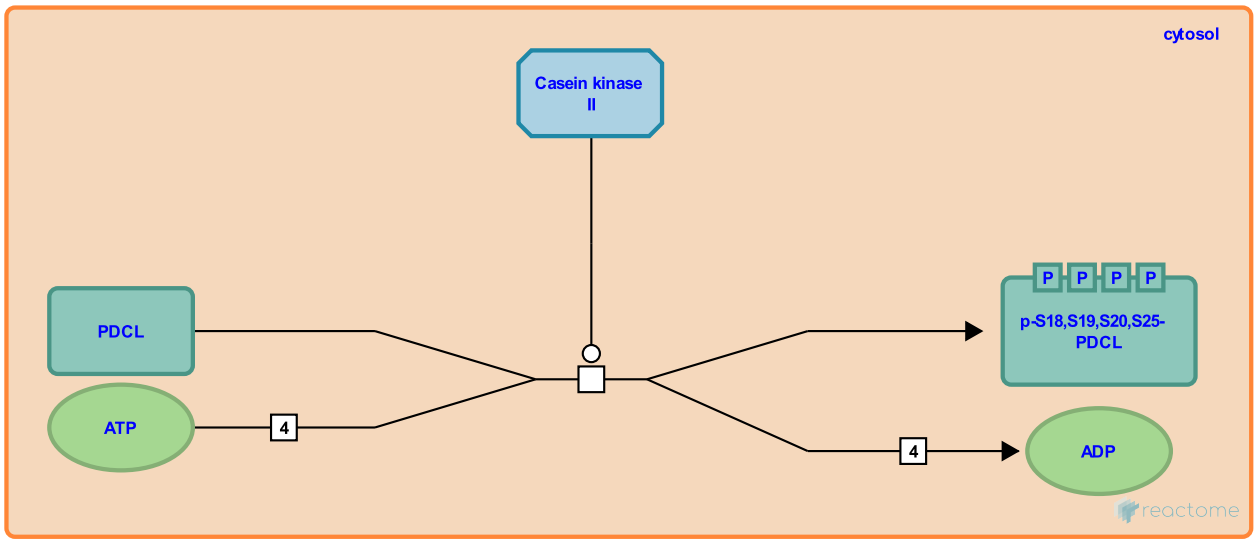
CK2 phosphorylates PDCL ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-6814409

Type: transition

Compartments: cytosol



The casein kinase II (CK2) complex phosphorylates PDCL (PhLP1) at the N-terminal serine residues S18, S19, S20 and S25. The phosphorylation at S20 is the most critical for PDCL-mediated folding of the G-protein beta subunit (Lukov et al. 2005, Lukov et al. 2006).

Followed by: PDCL binds G-protein beta and TRiC/CCT

Literature references

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. ↗

Lukov, GL., Hu, T., Hamm, HE., McLaughlin, JN., Willardson, BM. (2005). Phosducin-like protein acts as a molecular chaperone for G protein betagamma dimer assembly. *EMBO J., 24*, 1965-75. ↗

Editions

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

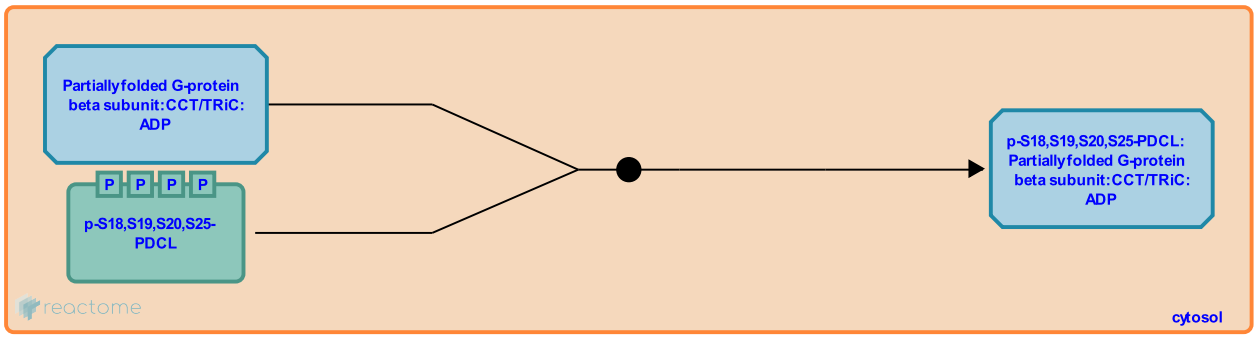
PDCL binds G-protein beta and TRiC/CCT ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-6814121

Type: binding

Compartments: cytosol



PDCL (PhLP1), phosphorylated by the casein kinase II complex (CK2), simultaneously binds to the unfolded G-protein beta subunit and the TRiC/CCT chaperonin (Lukov et al. 2005, Lukov et al. 2006, Plimpton et al. 2015). Phosphorylation is not a prerequisite for PDCL binding to TRiC/CCT and the unfolded G-protein beta, but is necessary for PDCL-mediated release of folded G-protein beta from TRiC/CCT (Lukov et al. 2006).

Preceded by: ATP hydrolysis promotes folding of G-protein beta by TRiC/CCT, CK2 phosphorylates PDCL

Followed by: PDCL promotes G-protein beta 5 folding, PDCL releases folded G-beta from TRiC/CCT

Literature references

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. ↗

Lukov, GL., Hu, T., Hamm, HE., McLaughlin, JN., Willardson, BM. (2005). Phosducin-like protein acts as a molecular chaperone for G protein betagamma dimer assembly. *EMBO J., 24*, 1965-75. ↗

Makaju, A., Lai, CW., Prince, JT., Carrascosa, JL., Plimpton, RL., Cuellar, J. et al. (2015). Structures of the Gβ-CCT and PhLP1-Gβ-CCT complexes reveal a mechanism for G-protein β-subunit folding and Gβγ dimer assembly. *Proc. Natl. Acad. Sci. U.S.A., 112*, 2413-8. ↗

Editions

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

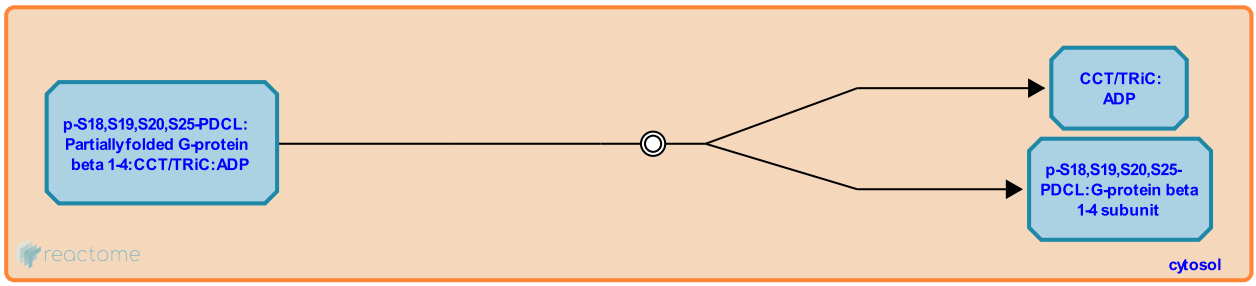
PDCL releases folded G-beta from TRiC/CCT ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-8850527

Type: dissociation

Compartments: cytosol



PDCL (PhLP1) enables completion of folding of G-protein beta subunits 1-4 (GNB1, GNB2, GNB3 and GNB4) by the TRiC/CCT chaperonin, resulting in the release of dimers of PDCL and folded G-protein beta 1-4 (Lukov et al. 2005, Lukov et al. 2006, Howlett et al. 2009, Plimpton et al. 2015).

Preceded by: PDCL binds G-protein beta and TRiC/CCT

Followed by: PDCL promotes formation of G-beta:G-gamma heterodimers

Literature references

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. ↗

Lukov, GL., Hu, T., Hamm, HE., McLaughlin, JN., Willardson, BM. (2005). Phosducin-like protein acts as a molecular chaperone for G protein betagamma dimer assembly. *EMBO J., 24*, 1965-75. ↗

Makaju, A., Lai, CW., Prince, JT., Carrascosa, JL., Plimpton, RL., Cuellar, J. et al. (2015). Structures of the Gβ-CCT and PhLP1-Gβ-CCT complexes reveal a mechanism for G-protein β-subunit folding and Gβγ dimer assembly. *Proc. Natl. Acad. Sci. U.S.A., 112*, 2413-8. ↗

Editions

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

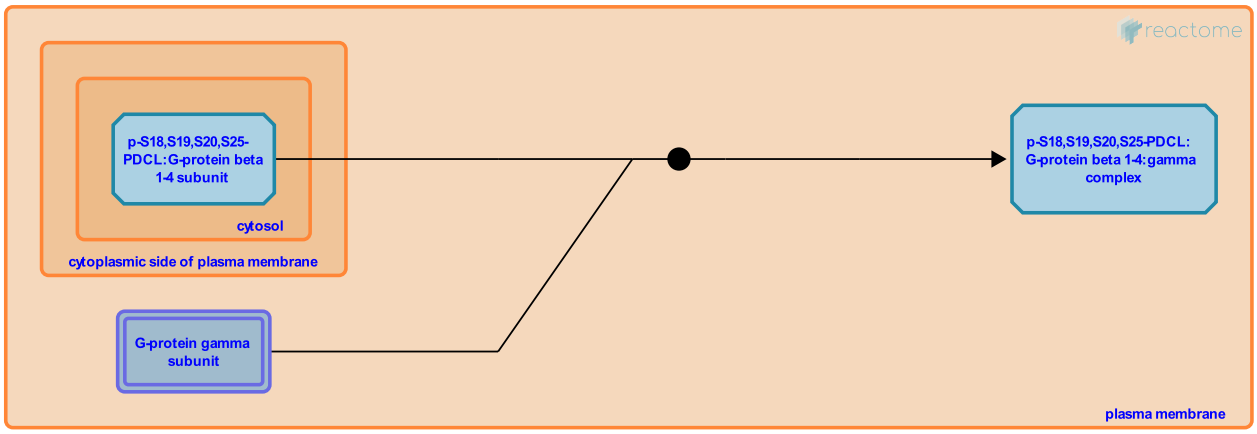
PDCL promotes formation of G-beta:G-gamma heterodimers ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-6814418

Type: binding

Compartments: plasma membrane, cytosol



G-protein gamma subunit binds folded G-protein beta subunits 1-4 associated with PDCL (PhLP1) after release from TRiC/CCT, resulting in formation of the G-protein beta:gamma complex (Lukov et al. 2006, Plimpton et al. 2015). In Pdcl-depleted mouse rods, G-protein beta:gamma dimer formation is decreased 50-fold, leading to 10-fold reduction in light sensitivity (Lai et al. 2013).

Preceded by: PDCL releases folded G-beta from TRiC/CCT

Followed by: G-protein alpha releases G-protein heterotrimer from PDCL

Literature references

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. ↗

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. ↗

Lukov, GL., Hu, T., Hamm, HE., McLaughlin, JN., Willardson, BM. (2005). Phosducin-like protein acts as a molecular chaperone for G protein betagamma dimer assembly. *EMBO J., 24*, 1965-75. ↗

Makaju, A., Lai, CW., Prince, JT., Carrascosa, JL., Plimpton, RL., Cuellar, J. et al. (2015). Structures of the Gβ-CCT and PhLP1-Gβ-CCT complexes reveal a mechanism for G-protein β-subunit folding and Gβγ dimer assembly. *Proc. Natl. Acad. Sci. U.S.A., 112*, 2413-8. ↗

Editions

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

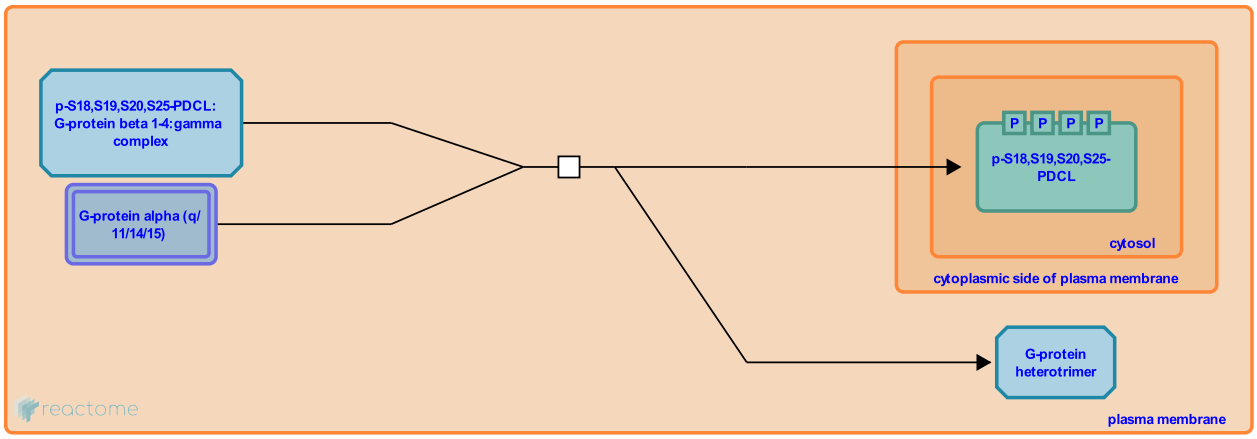
G-protein alpha releases G-protein heterotrimer from PDCL ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-8850560

Type: transition

Compartments: plasma membrane, cytosol



G-protein alpha associates with G-protein beta:gamma dimers bound to PDCL (PhLP1), resulting in release of the G-protein heterotrimer from PDCL co-chaperone (Lukov et al. 2005, Plimpton et al. 2015).

Preceded by: PDCL promotes formation of G-beta:G-gamma heterodimers

Literature references

Lukov, GL., Hu, T., Hamm, HE., McLaughlin, JN., Willardson, BM. (2005). Phosducin-like protein acts as a molecular chaperone for G protein betagamma dimer assembly. *EMBO J., 24*, 1965-75. ↗

Makaju, A., Lai, CW., Prince, JT., Carrascosa, JL., Plimpton, RL., Cuellar, J. et al. (2015). Structures of the Gβ-CCT and PhLP1-Gβ-CCT complexes reveal a mechanism for G-protein β-subunit folding and Gβγ dimer assembly. *Proc. Natl. Acad. Sci. U.S.A., 112*, 2413-8. ↗

Editions

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

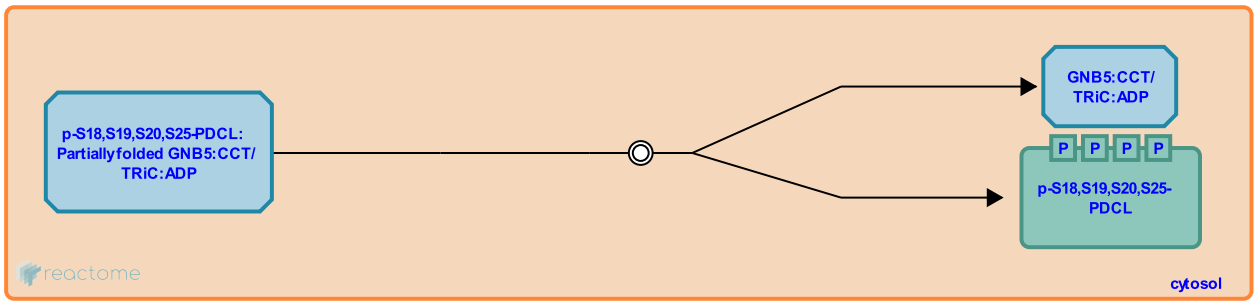
PDCL promotes G-protein beta 5 folding ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-8850534

Type: dissociation

Compartments: cytosol



PDCL (PhLP1) increases stability of the G-protein beta 5 subunit (GNB5), presumably by assisting with the proper folding of GNB5, but does not release folded GNB5 from the TRiC/CCT chaperonin (Howlett et al. 2009).

Preceded by: PDCL binds G-protein beta and TRiC/CCT

Followed by: RGS proteins bind GNB5 and CCT/TRiC

Literature references

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. ↗

Editions

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

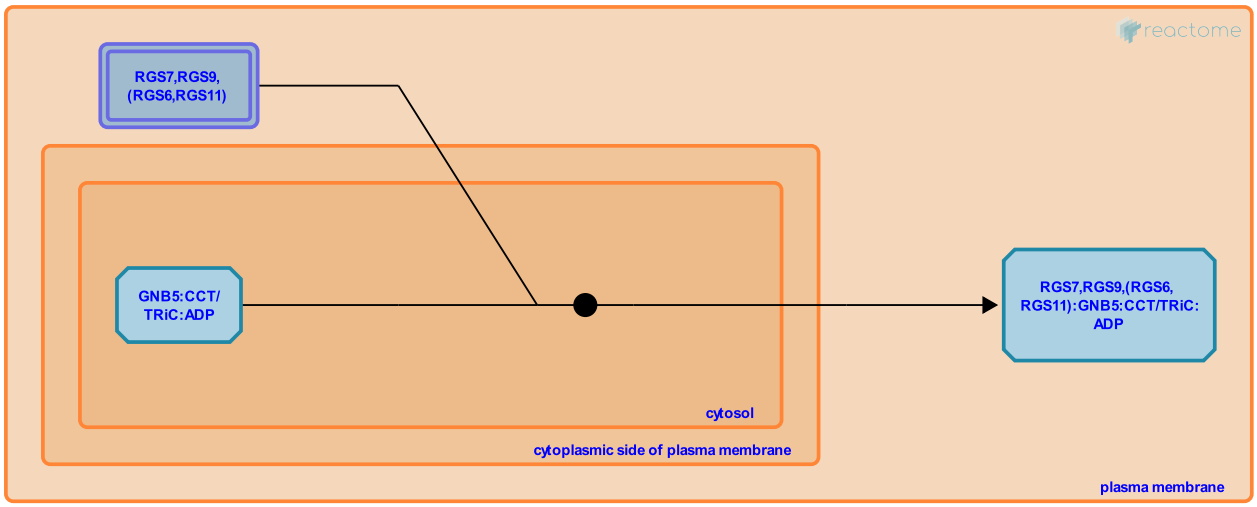
RGS proteins bind GNB5 and CCT/TRiC ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-8850529

Type: binding

Compartments: cytosol



RGS proteins RGS7, RGS9 and, probably RGS6 and RGS11, bind to folded G-protein beta 5 subunit (GNB5) associated with the CCT/TRiC chaperonin. A RGS protein can associate with GNB5 and CCT/TRiC only after PDCL (PhLP1) is released as PDCL and RGS protein interact with overlapping regions of GNB5 (Howlett et al. 2009, Tracy et al. 2015).

Preceded by: PDCL promotes G-protein beta 5 folding

Followed by: Release of GNB5:RGS dimers from CCT/TRiC

Literature references

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. ↗

Chen, CK., Baehr, W., Kolesnikov, AV., Tracy, CM., Blake, DR., Kefalov, VJ. et al. (2015). Retinal cone photoreceptors require phosducin-like protein 1 for G protein complex assembly and signaling. *PLoS ONE, 10*, e0117129. ↗

Editions

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

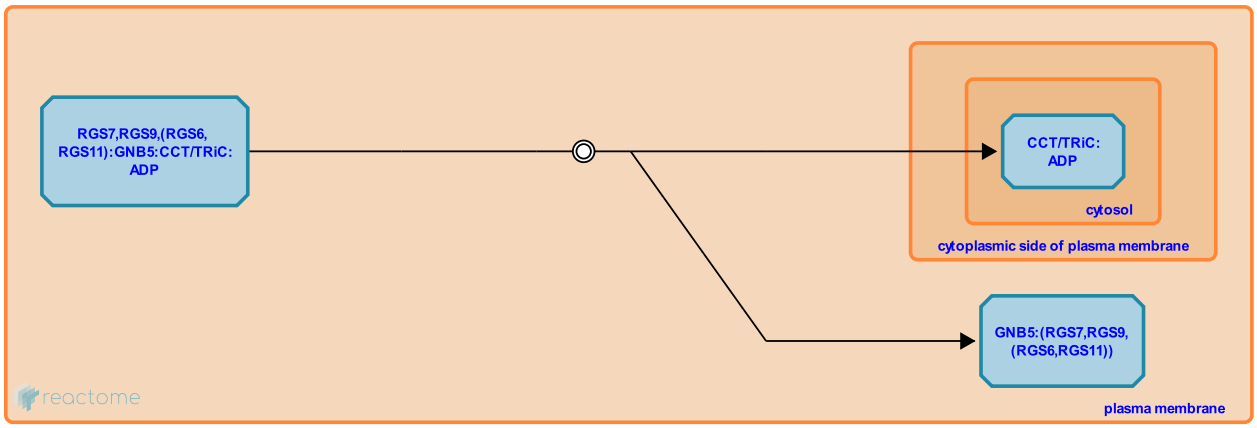
Release of GNB5:RGS dimers from CCT/TRiC ↗

Location: Cooperation of PDCL (PhLP1) and TRiC/CCT in G-protein beta folding

Stable identifier: R-HSA-8850539

Type: dissociation

Compartments: plasma membrane, cytosol



Dimers of folded G-protein beta 5 subunit (GNB5) and a RGS protein RGS7, RSG9, and probably RGS6 or RGS11, are released from the CCT/TRiC chaperonin complex (Howlett et al. 2009, Tracy et al. 2015).

Preceded by: RGS proteins bind GNB5 and CCT/TRiC

Literature references

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. ↗

Chen, CK., Baehr, W., Kolesnikov, AV., Tracy, CM., Blake, DR., Kefalov, VJ. et al. (2015). Retinal cone photoreceptors require phosducin-like protein 1 for G protein complex assembly and signaling. *PLoS ONE, 10*, e0117129. ↗

Editions

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

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