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

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13/08/2019
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


Reactome database release: 69

This document contains 1 pathway and 11 reactions (see Table of Contents)
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


Editions

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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


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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

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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

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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

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https://reactome.org
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:** CK2 phosphorylates PDCL, ATP hydrolysis promotes folding of G-protein beta by TRiC/CCT

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

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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


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

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

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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: cytosol, plasma membrane


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

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

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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:** cytosol, plasma membrane

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

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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

**Compartment:** 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

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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

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**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:** cytosol, plasma membrane

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

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  - CK2 phosphorylates PDCL
  - PDCL binds G-protein beta and TRiC/CCT
  - PDCL releases folded G-beta from TRiC/CCT
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