

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. [↗](#)

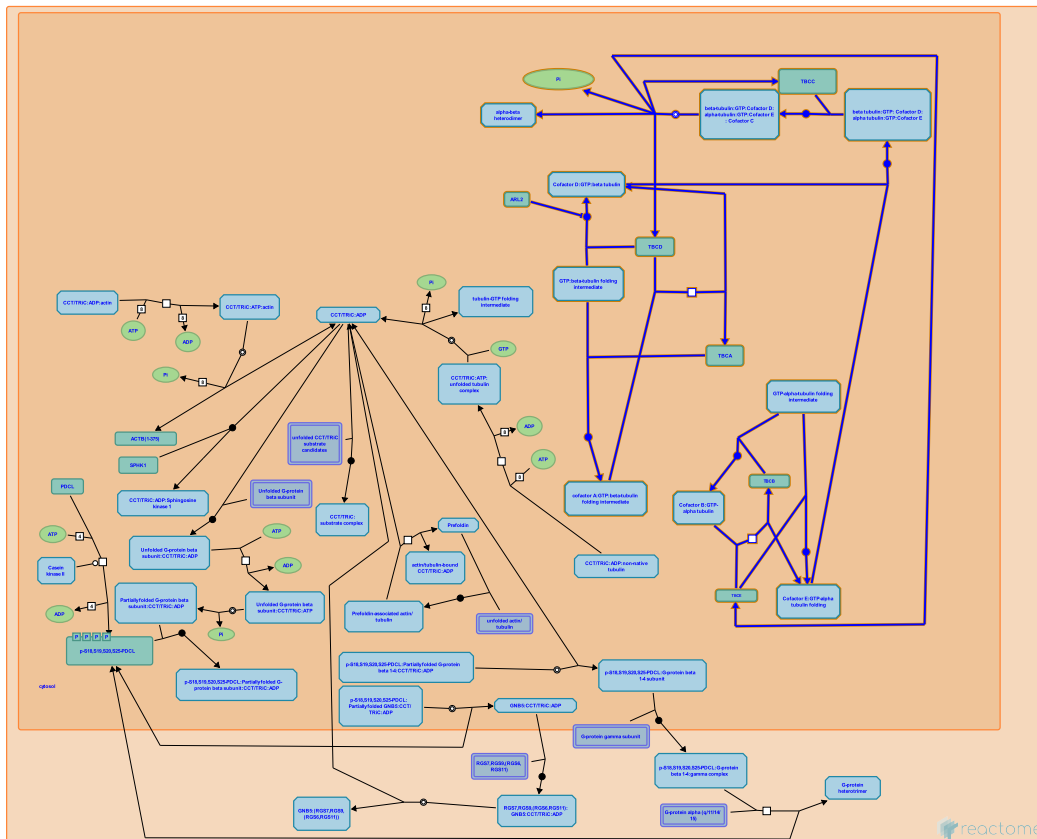
Reactome database release: 88

This document contains 1 pathway and 9 reactions ([see Table of Contents](#))

Post-chaperonin tubulin folding pathway ↗

Stable identifier: R-HSA-389977

Compartments: cytosol



Alpha and beta tubulin folding intermediates are formed through ATP-dependent interaction with TriC/CCT. In order to form a functional heterodimer, these folding intermediates undergo a series of interactions with five proteins: (cofactors A-E) following release from TriC/CCT (reviewed in Cowan and Lewis et al., 2001). These interactions are described in the reactions below. Ultimately, alpha tubulin, when associated with cofactor E, interacts with cofactor D-bound beta-tubulin. The entry of cofactor C into this complex results in the discharge of native heterodimer triggered by GTP hydrolysis in beta tubulin (Tian et al., 1997).

Literature references

Lewis, SA., Cowan, NJ., Tian, G. (1997). The alpha- and beta-tubulin folding pathways. *Trends Cell Biol*, 7, 479-84. ↗

Editions

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

Beta-tubulin:GTP + Cofactor A -> Beta-tubulin:GTP: Cofactor A ↗

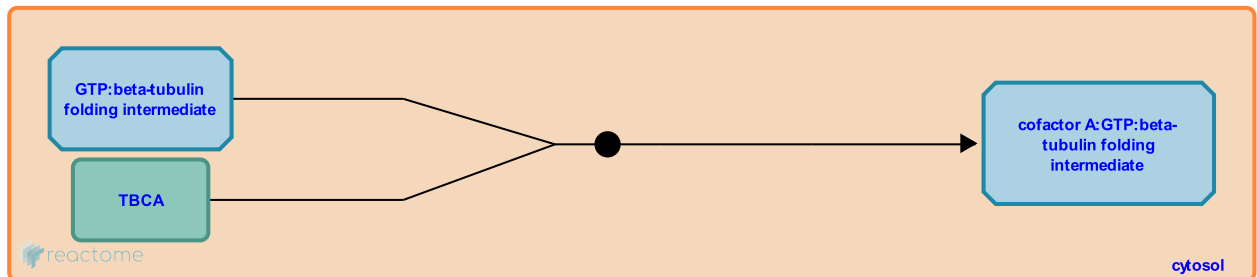
Location: [Post-chaperonin tubulin folding pathway](#)

Stable identifier: R-HSA-389956

Type: binding

Compartments: cytosol

Inferred from: [Beta-tubulin:GTP + Cofactor A -> Beta-tubulin:GTP: Cofactor A \(Bos taurus\)](#)



Beta-tubulin folding intermediates generated via ATP-dependent interaction with TriC/CCT are captured by tubulin-specific chaperones A and D (TBCA and TBCD) (Tian et al. 1996, Tian et al. 1997) in a reversible reaction forming tubulin intermediate/cofactor complexes Factor A:beta tubulin or Factor D:beta tubulin. TBCD is involved in the tubulin-folding pathway, acting as a GTPase activating protein (GAP) for beta-tubulin. The ADP-ribosylation factor-like protein 2 (ARL2) is able to down-regulate TBCD specifically, thus preventing microtubule disruption (Bhamidipati et al. 2000, Tian et al. 2010).

Followed by: [Beta-tubulin:GTP: Cofactor A+ Cofactor D -> Beta-tubulin:GTP:Cofactor D + Cofactor A](#)

Editions

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

Beta-tubulin:GTP + Cofactor D -> Beta-tubulin:GTP: Cofactor D ↗

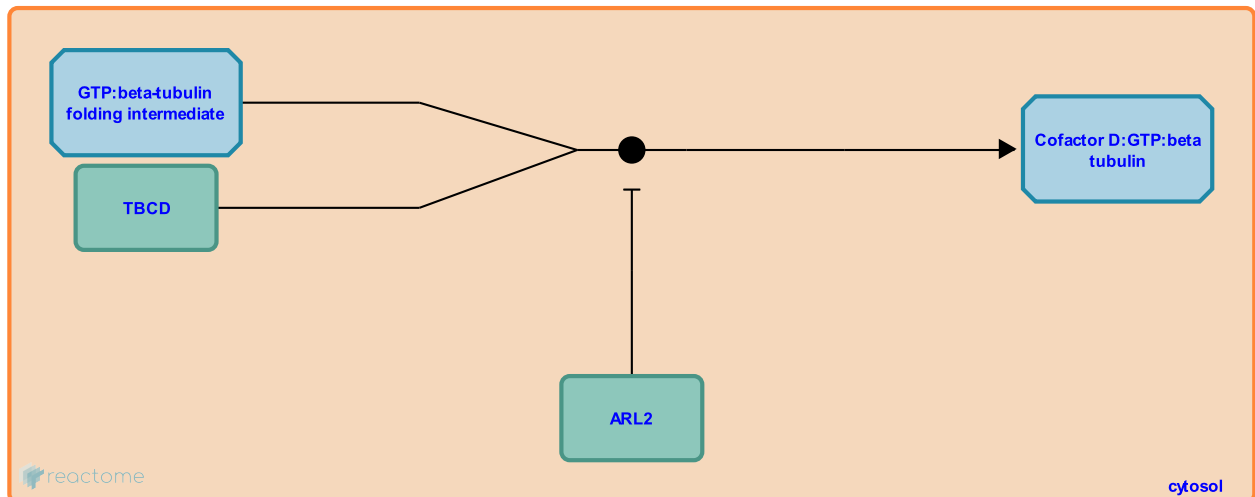
Location: [Post-chaperonin tubulin folding pathway](#)

Stable identifier: R-HSA-389969

Type: binding

Compartments: cytosol

Inferred from: [Beta-tubulin:GTP + Cofactor D -> Beta-tubulin:GTP: Cofactor D \(Bos taurus\)](#)



Beta-tubulin folding intermediates generated via ATP-dependent interaction with TriC/CCT are captured by tubulin-specific chaperones A and D (TBCA and TBCD) (Tian et al. 1996, Tian et al. 1997) in a reversible reaction forming tubulin intermediate/cofactor complexes Factor A:beta tubulin or Factor D:beta tubulin. TBCD is involved in the tubulin-folding pathway, acting as a GTPase activating protein (GAP) for beta-tubulin. The ADP-ribosylation factor-like protein 2 (ARL2) is able to down-regulate TBCD specifically, thus preventing microtubule disruption (Bhamidipati et al. 2000, Tian et al. 2010).

Followed by: [Beta-tubulin:GTP:Cofactor D+alpha-tubulin:GTP:Cofactor E-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E](#)

Literature references

Lewis, SA., Cowan, NJ., Bhamidipati, A. (2000). ADP ribosylation factor-like protein 2 (Arl2) regulates the interaction of tubulin-folding cofactor D with native tubulin. *J. Cell Biol.*, 149, 1087-96. ↗

Cowan, NJ., Tian, G., Thomas, S. (2010). Effect of TBCD and its regulatory interactor Arl2 on tubulin and microtubule integrity. *Cytoskeleton (Hoboken)*, 67, 706-14. ↗

Editions

2008-12-01	Authored	Matthews, L.
2009-01-21	Reviewed	Cowan, NJ.
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2015-02-11	Revised	Jassal, B.

Beta-tubulin:GTP: Cofactor A+ Cofactor D -> Beta-tubulin:GTP:Cofactor D + Cofactor A ↗

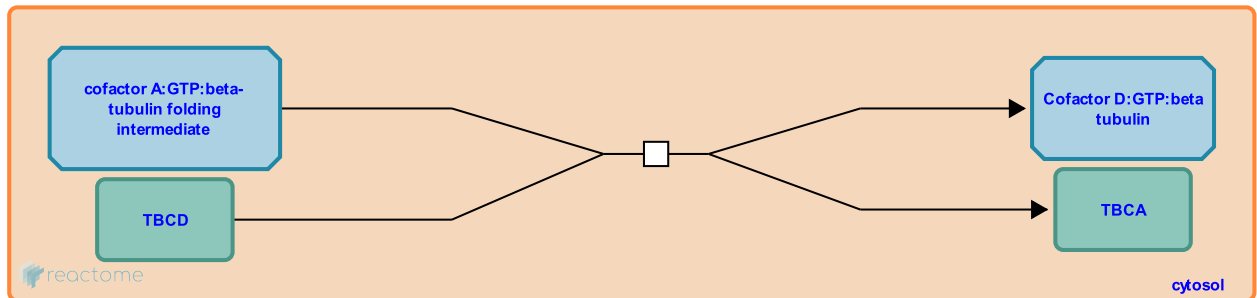
Location: Post-chaperonin tubulin folding pathway

Stable identifier: R-HSA-389955

Type: transition

Compartments: cytosol

Inferred from: Beta-tubulin:GTP: Cofactor A+ Cofactor D -> Beta-tubulin:GTP:Cofactor D + Cofactor A (Bos taurus)



Factor A:beta tubulin complex act as a reservoir capable of accepting or delivering its target tubulin protein to cofactor D (Tian et al., 1997). In the reverse reaction, Cofactor A may displace cofactor D in a cofactor D:beta tubulin complex.

Preceded by: Beta-tubulin:GTP + Cofactor A -> Beta-tubulin:GTP: Cofactor A

Followed by: Beta-tubulin:GTP:Cofactor D+alpha-tubulin:GTP:Cofactor E-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E

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

alpha-tubulin:GTP + Cofactor B -> alpha-tubulin:GTP: Cofactor B ↗

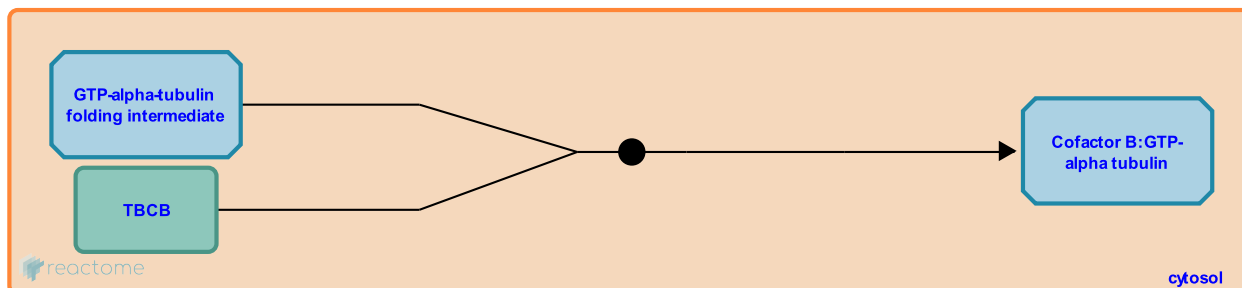
Location: [Post-chaperonin tubulin folding pathway](#)

Stable identifier: R-HSA-389972

Type: binding

Compartments: cytosol

Inferred from: [alpha-tubulin:GTP + Cofactor B -> alpha-tubulin:GTP: Cofactor B \(Bos taurus\)](#)



Quasi-native alpha-tubulin folding intermediates generated via ATP-dependent interaction with CCT (Tian et al., 1995) are captured in a reversible reaction by cofactors B and/or E (Tian et al., 1997), forming the tubulin intermediate/cofactor complexes Factor B:alpha tubulin or Factor E:alpha tubulin.

Followed by: [alpha-tubulin:GTP:Cofactor B +Cofactor E -> alpha-tubulin:GTP: Cofactor E +Cofactor B](#)

Editions

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

alpha-tubulin:GTP + Cofactor E -> alpha-tubulin:GTP:Cofactor E ↗

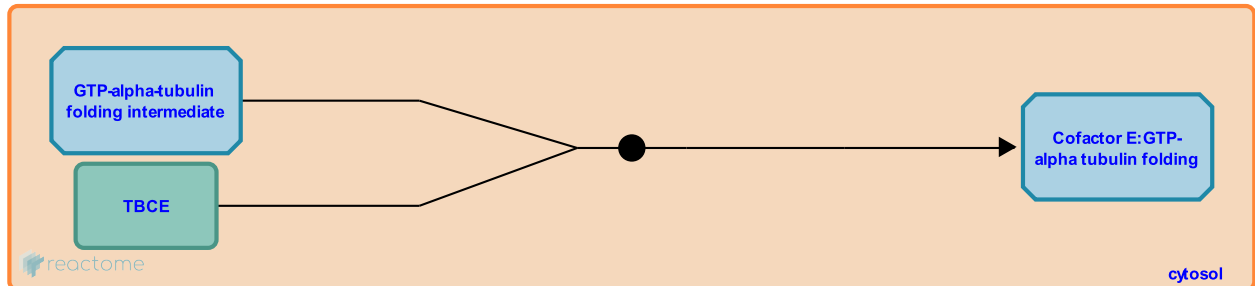
Location: [Post-chaperonin tubulin folding pathway](#)

Stable identifier: R-HSA-389978

Type: binding

Compartments: cytosol

Inferred from: [alpha-tubulin:GTP + Cofactor E -> alpha-tubulin:GTP:Cofactor E \(Bos taurus\)](#)



Quasi-native alpha-tubulin folding intermediates generated via ATP-dependent interaction with CCT (Tian et al., 1995) are captured in a reversible reaction by cofactors B and/or E (Tian et al., 1997), forming the tubulin intermediate/cofactor complexes Factor B:alpha tubulin or Factor E:alpha tubulin.

Followed by: [Beta-tubulin:GTP:Cofactor D+alpha-tubulin:GTP:Cofactor E-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E](#)

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

alpha-tubulin:GTP:Cofactor B +Cofactor E -> alpha-tubulin:GTP: Cofactor E +Cofactor B ↗

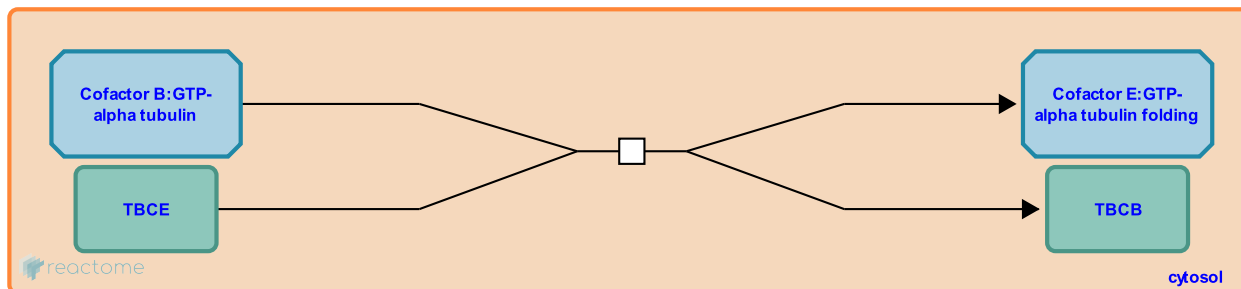
Location: [Post-chaperonin tubulin folding pathway](#)

Stable identifier: R-HSA-389963

Type: transition

Compartments: cytosol

Inferred from: [alpha-tubulin:GTP + Cofactor B -> alpha-tubulin:GTP: Cofactor B \(Bos taurus\)](#)



The factor B:alpha tubulin complex act as a reservoir capable of accepting or delivering alpha tubulin to cofactor E (Tian et al., 1997). In the reverse reaction, cofactor B may displace cofactor E in the cofactor E:alpha tubulin complex.

Preceded by: [alpha-tubulin:GTP + Cofactor B -> alpha-tubulin:GTP: Cofactor B](#)

Followed by: [Beta-tubulin:GTP:Cofactor D+alpha-tubulin:GTP:Cofactor E-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E](#)

Literature references

Rommelaere, H., Lewis, SA., Stearns, T., Cowan, NJ., Feierbach, B., Tian, G. et al. (1997). Tubulin subunits exist in an activated conformational state generated and maintained by protein cofactors. *J Cell Biol*, 138, 821-32. ↗

Editions

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

Beta-tubulin:GTP:Cofactor D+alpha-tubulin:GTP:Cofactor E-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E ↗

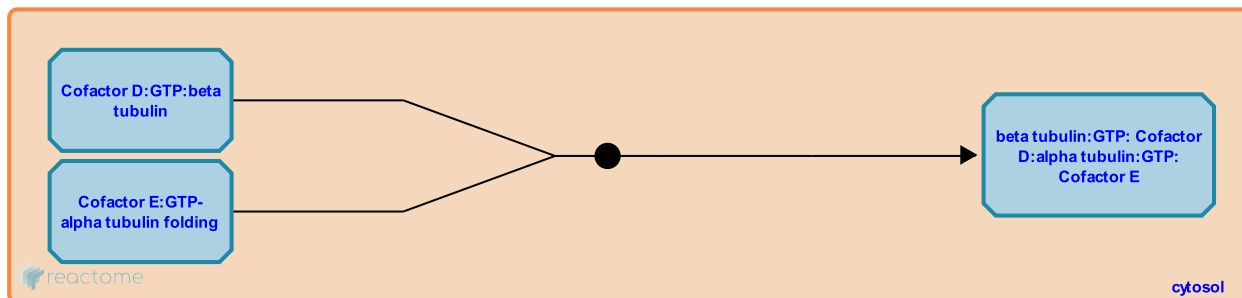
Location: [Post-chaperonin tubulin folding pathway](#)

Stable identifier: R-HSA-389976

Type: binding

Compartments: cytosol

Inferred from: [Beta-tubulin:GTP:Cofactor D+alpha-tubulin:GTP:Cofactor E-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E \(Bos taurus\)](#)



Factor E:alpha tubulin and Factor D:beta tubulin interact with each other in a reversible reaction to form the complex (Factor E alpha tubulin:Factor D:beta tubulin) (Tian et al., 1997).

Preceded by: [alpha-tubulin:GTP + Cofactor E -> alpha-tubulin:GTP:Cofactor E](#), [alpha-tubulin:GTP:Cofactor B +Cofactor E -> alpha-tubulin:GTP: Cofactor E +Cofactor B](#), [Beta-tubulin:GTP:Cofactor A+ Cofactor D -> Beta-tubulin:GTP:Cofactor D + Cofactor A](#), [Beta-tubulin:GTP + Cofactor D -> Beta-tubulin:GTP: Cofactor D](#)

Followed by: [Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E+ Cofactor C-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E:Cofactor C](#)

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2008-12-01	Authored	Matthews, L.
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Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E+ Cofactor C-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E:Cofactor C ↗

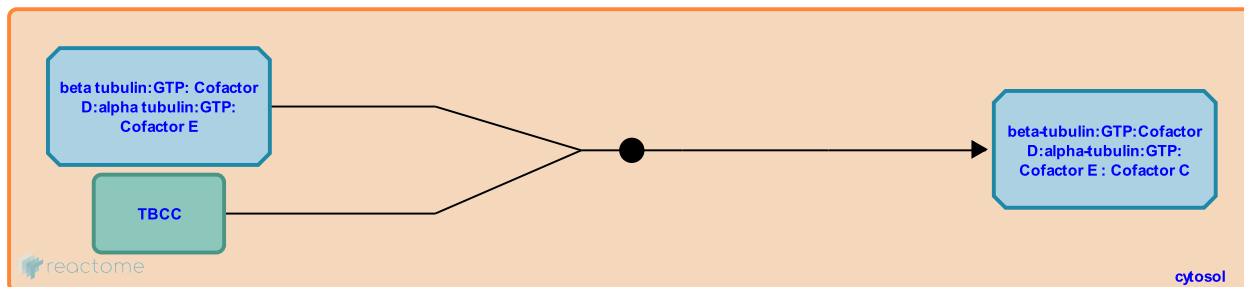
Location: [Post-chaperonin tubulin folding pathway](#)

Stable identifier: R-HSA-389964

Type: binding

Compartments: cytosol

Inferred from: [Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E+ Cofactor C-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E:Cofactor C \(Bos taurus\)](#)



Entry of cofactor C to the factor E:alpha tubulin: factor D:beta tubulin complex generates the active alpha:beta-supercomplex (Tian et al., 1997).

Preceded by: [Beta-tubulin:GTP:Cofactor D+alpha-tubulin:GTP:Cofactor E-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E](#)

Followed by: [Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E:Cofactor C-> Beta-tubulin:GDP :alpha-tubulin:GTP heterodimer +Cofactor E+ Cofactor D+ Cofactor C+ Pi](#)

Literature references

Rommelaere, H., Lewis, SA., Stearns, T., Cowan, NJ., Feierbach, B., Tian, G. et al. (1997). Tubulin subunits exist in an activated conformational state generated and maintained by protein cofactors. *J Cell Biol*, 138, 821-32. ↗

Editions

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

Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E:Cofactor C-> Beta-tubulin:GDP :alpha-tubulin:GTP heterodimer +Cofactor E+ Cofactor D+ Cofactor C+ Pi

↗

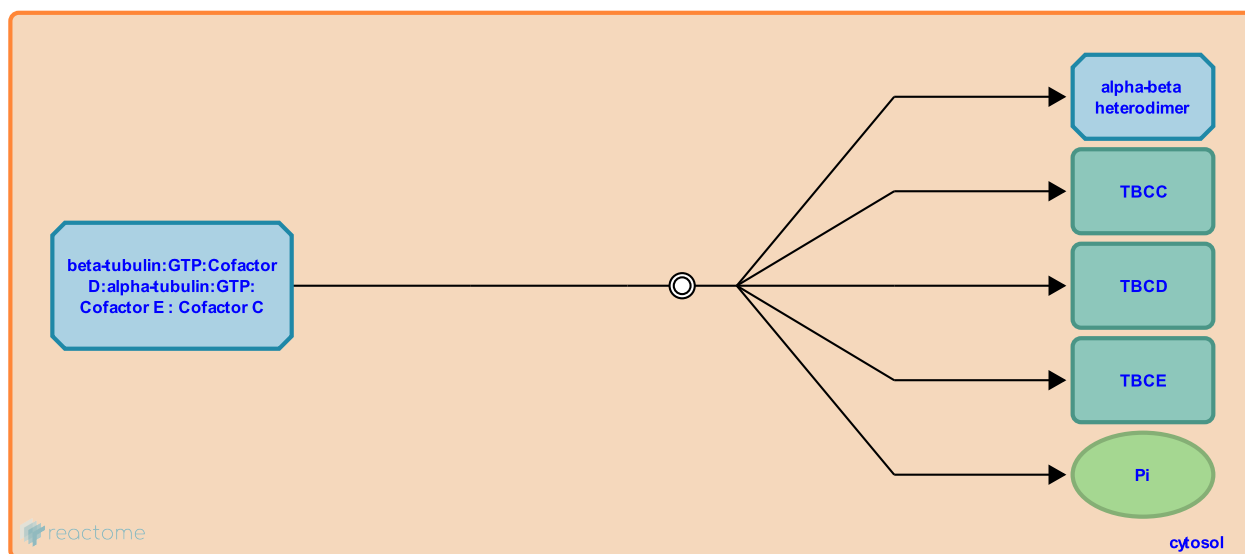
Location: [Post-chaperonin tubulin folding pathway](#)

Stable identifier: R-HSA-389974

Type: dissociation

Compartments: cytosol

Inferred from: [Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E:Cofactor C-> Beta-tubulin:GDP :alpha-tubulin:GTP heterodimer +Cofactor E+ Cofactor D+ Cofactor C+ Pi \(Bos taurus\)](#)



Beta tubulin within the active (Factor E:alpha tubulin: Factor D:beta tubulin:Factor C)-supercomplex hydrolyzes GTP. This results in the dissociation of the complex and the release of the native tubulin heterodimer (Tian et al., 1997).

Preceded by: [Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E+ Cofactor C-> Beta-tubulin:GTP:Cofactor D:alpha-tubulin:GTP:Cofactor E:Cofactor C](#)

Editions

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