Regulation of PLK1 Activity at G2/M Transition

Bruinsma, W., Orlic-Milacic, M., Weil, R.

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

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22/07/2019
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 12 reactions (see Table of Contents)
Regulation of PLK1 Activity at G2/M Transition

Stable identifier: R-HSA-2565942

Compartments: cytosol

The kinase activity of PLK1 is required for cell cycle progression as PLK1 phosphorylates and regulates a number of cellular proteins during mitosis. Centrosomic AURKA (Aurora A kinase), catalytically activated through AJUBA facilitated autophosphorylation on threonine residue T288 at G2/M transition (Hirota et al. 2003), activates PLK1 on centrosomes by phosphorylating threonine residue T210 of PLK1, critical for PLK1 activity (Jang et al. 2002), in the presence of BORA (Macurek et al. 2008, Seki et al. 2008). Once activated, PLK1 phosphorylates BORA and targets it for ubiquitination mediated degradation by SCF-beta-TrCP ubiquitin ligases. Degradation of BORA is thought to allow PLK1 to interact with other substrates (Seki, Coppinger, Du et al. 2008, Seki et al. 2008).

The interaction of PLK1 with OPTN (optineurin) provides a negative-feedback mechanism for regulation of PLK1 activity. Phosphorylated PLK1 binds and phosphorylates OPTN associated with the Golgi membrane GTPase RAB8, promoting dissociation of OPTN from Golgi and translocation of OPTN to the nucleus. Phosphorylated OPTN facilitates the mitotic phosphorylation of the myosin phosphatase subunit PPP1R12A (MYPT1) and myosin phosphatase activation (Kachaner et al. 2012). The myosin phosphatase complex dephosphorylates threonine residue T210 of PLK1 and inactivates PLK1 (Yamashiro et al. 2008).

Literature references


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AJUBA binds centrosome-associated AURKA

**Location:** Regulation of PLK1 Activity at G2/M Transition

**Stable identifier:** R-HSA-2574845

**Type:** binding

**Compartments:** cytosol

AJUBA, a LIM domain-containing protein, binds centrosome-associated AURKA (Aurora A kinase) through interaction of LIM-2 and LIM-3 domains of AJUBA with the N-terminus of AURKA (Hirota et al. 2003).

**Followed by:** AJUBA facilitates AURKA autophosphorylation

**Literature references**


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AJUBA facilitates AURKA autophosphorylation

**Location:** Regulation of PLK1 Activity at G2/M Transition

**Stable identifier:** R-HSA-2574840

**Type:** transition

**Compartments:** cytosol

AURKA (Aurora A kinase) activation through autophosphorylation of threonine T288 is facilitated by AJUBA binding. AJUBA is also phosphorylated by AURKA on an unidentified serine or threonine residue (Hirota et al. 2003).

**Preceded by:** AJUBA binds centrosome-associated AURKA

**Followed by:** BORA binds PLK1 and AURKA

**Literature references**


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CDK1 phosphorylates BORA

**Location:** Regulation of PLK1 Activity at G2/M Transition

**Stable identifier:** R-HSA-4086410

**Type:** transition

**Compartments:** cytosol

CDK1 phosphorylates both human and Drosophila BORA protein (Hutterer et al. 2006) on an evolutionarily conserved serine residue - S252 in human BORA (Chan et al. 2008), providing a docking site for PLK1.

**Followed by:** BORA binds PLK1 and AURKA

**Literature references**


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BORA binds PLK1 and AURKA

Location: Regulation of PLK1 Activity at G2/M Transition

Stable identifier: R-HSA-3000319

Type: binding

Compartments: cytosol

BORA is able to interact with both AURKA (Aurora A kinase) and PLK1. Binding of BORA to PLK1 increases the accessibility of PLK1 threonine residue T210 and also brings PLK1 in proximity to AURKA, enabling AURKA to phosphorylate T210 of PLK1 and thereby activate PLK1 (Seki et al. 2008). While BORA is required for mitotic activation of AURKA in Drosophila (Hutterer et al. 2006), it does not significantly activate AURKA in human cells (Seki et al. 2008). AURKA is able to phosphorylate BORA in vitro, but the functional significance of this modification has not been determined (Hutterer et al. 2006).

Preceded by: CDK1 phosphorylates BORA, AJUBA facilitates AURKA autophosphorylation

Followed by: AURKA phosphorylates PLK1

Literature references


Editions

- 2013-01-29: Authored by Orlic-Milacic, M.
- 2013-01-30: Edited by Orlic-Milacic, M.
- 2013-08-21: Reviewed by Bruinsma, W.
AURKA phosphorylates PLK1

Location: Regulation of PLK1 Activity at G2/M Transition

Stable identifier: R-HSA-3000310

Type: transition

Compartments: cytosol

AURKA (Aurora A kinase) phosphorylates PLK1 on threonine residue T210 that lies in the conserved aurora kinase consensus site (Seki et al. 2008). PLK1 needs to be phosphorylated on T210 to become catalytically active (Jang et al. 2002). BORA, but not other AURKA co-activators, facilitate PLK1 phosphorylation by AURKA (Macurek et al. 2008, Seki et al. 2008).

Preceded by: BORA binds PLK1 and AURKA

Followed by: PLK1 phosphorylates OPTN, PLK1 phosphorylates BORA

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PLK1 phosphorylates BORA

Location: Regulation of PLK1 Activity at G2/M Transition

Stable identifier: R-HSA-3000327

Type: transition

Compartments: cytosol

PLK1 phosphorylates BORA on serine residue S497 and threonine residue T501 that both lie in the DS-GYNT degron recognized by beta-TrCP F-box proteins (Seki et al. 2008).

Preceded by: AURKA phosphorylates PLK1

Followed by: Phosphorylated BORA binds SCF-beta-TrCp1/2, Cytosolic PLK1 translocates to the nucleus

Literature references

Phosphorylated BORA binds SCF-beta-TrCp1/2

Location: Regulation of PLK1 Activity at G2/M Transition

Stable identifier: R-HSA-3000339

Type: binding

Compartments: cytosol

The substrate recognition subunits beta-TrCP (BTRC) and beta-TrCP2 (FBXW11) of SCF-beta-TrPC1 and SCF-beta-TrPC2 ubiquitin ligases, respectively, bind the phosphorylated DSGYNT motif of BORA (Seki et al. 2008).

Preceded by: PLK1 phosphorylates BORA

Followed by: SCF-beta-TrCp1/2 ubiquitinates phosphorylated BORA

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SCF-beta-TrCP1/2 ubiquitinates phosphorylated BORA

Location: Regulation of PLK1 Activity at G2/M Transition

Stable identifier: R-HSA-3000335

Type: transition

Compartments: cytosol

SCF-beta-TrCP ubiquitin ligases promote ubiquitination and degradation of BORA phosphorylated by PLK1, and this is required for timely mitotic progression (Seki et al. 2008).

Preceded by: Phosphorylated BORA binds SCF-beta-TrCp1/2

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Activated PLK1 phosphorylates OPTN (optineurin) on serine residue S177. Phosphorylation at S177 disrupts OPTN binding to Golgi-membrane localized RAB8A (Kachaner et al. 2012).

**Preceded by:** AURKA phosphorylates PLK1  
**Followed by:** Phosphorylated OPTN translocates to the nucleus

**Literature references**

Phosphorylated OPTN translocates to the nucleus

**Location:** Regulation of PLK1 Activity at G2/M Transition

**Stable identifier:** R-HSA-2562594

**Type:** transition

**Compartments:** cytosol, nucleoplasm

Phosphorylation of OPTN (optineurin) on serine S177 by PLK1 promotes translocation of OPTN to the nucleus (Kachaner et al. 2012).

**Preceded by:** PLK1 phosphorylates OPTN

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Cytosolic PLK1 translocates to the nucleus

**Location:** Regulation of PLK1 Activity at G2/M Transition

**Stable identifier:** R-HSA-3002798

**Type:** transition

**Compartments:** cytosol, nucleoplasm

PLK1 is induced in S phase and can be find in both cytosol and nucleus in S and G2 phases of the cell cycle. PLK1 possesses a bipartite nuclear localization signal (NLS) that enables it to enter the nucleus (Taniguchi et al. 2002).

**Preceded by:** PLK1 phosphorylates BORA

**Followed by:** Myosin phosphatase dephosphorylates PLK1

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Myosin phosphatase dephosphorylates PLK1

Location: Regulation of PLK1 Activity at G2/M Transition

Stable identifier: R-HSA-3002811

Type: transition

Compartments: nucleoplasm

The myosin phosphatase complex can dephosphorylate PLK1 threonine residue T210 and inactivate PLK1 (Yamashiro et al. 2008). Myosin phosphatase is activated through phosphorylation of its PPP1R12A (MYPT1) subunit. Several kinases, including CDK1 (Yamashiro et al. 2008) and LATS1 (Chiyoda et al. 2012) have been implicated in myosin phosphatase activation, but the position and temporal order of key PPP1R12A phosphorylations need to be investigated further. Phosphorylated OPTN (optineurin) is able to bind PPP1R12A (MYPT1) and positively regulates PLK1 dephosphorylation by myosin phosphatase, possibly by facilitating PPP1R12A phosphorylation and myosin phosphatase activation (Kachaner et al. 2012).

Preceded by: Cytosolic PLK1 translocates to the nucleus

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