Golgi Cisternae Pericentriolar Stack Reorganization


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18/11/2022
Introduction

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Literature references


Reactome database release: 82

This document contains 1 pathway and 6 reactions (see Table of Contents)

https://reactome.org
The pericentriolar stacks of Golgi cisternae undergo extensive fragmentation and reorganization in mitosis.

In mammalian cells, Golgi apparatus consists of stacked cisternae that are connected by tubules to form a ribbon-like structure in the perinuclear region, in vicinity of the centrosome. Reorganization of the Golgi apparatus during cell division allows both daughter cells to inherit this organelle, and may play additional roles in the organization of the mitotic spindle.

First changes in the structure of the Golgi apparatus likely start in G2 and are subtle, involving unlinking of the Golgi ribbon into separate stacks. These changes are required for the entry of mammalian cells into mitosis (Sutterlin et al. 2002). This initial unlinking of the Golgi ribbon depends on GRASP proteins and on CTBP1 (BARS) protein, which induces the cleavage of the tubular membranes connecting the stacks (Hidalgo Carcedo et al. 2004, Colanzi et al. 2007), but the exact mechanism is not known. Activation of MEK1/2 also contributes to unlinking of the Golgi ribbon in G2 (Feinstein and Linsteadt 2007).

From prophase to metaphase, Golgi cisternae undergo extensive fragmentation that is a consequence of unstacking of Golgi cisternae and cessation of transport through Golgi. At least three mitotic kinases, CDK1, PLK1 and MEK1, regulate these changes. CDK1 in complex with cyclin B phosphorylates GOLGA2 (GM130) and GORASP1 (GRASP65), constituents of a cis-Golgi membrane complex (Lowe et al. 1998, Preisinger et al. 2005). Phosphorylation of GOLGA2 prevents binding of USO1 (p115), a protein localizing to the membrane of ER (endoplasmic reticulum) to Golgi transport vesicles and cis-Golgi, thereby impairing fusion of these vesicles with cis-Golgi cisternae and stopping ER to Golgi transport (Lowe et al. 1998,

In the median Golgi, GORASP2 (GRASP55), a protein that forms a complex with BLFZ1 (Golgin-45) and RAB2A GTPase and contributes to cisternae stacking and Golgi trafficking (Short et al. 2001), is also phosphorylated in mitosis. Phosphorylation of GORASP2 by MEK1/2-activated MAPK1 (ERK2) and/or MAPK3-3 (ERK1b in human, Erk1c in rat) contributes to Golgi unlinking in G2 and fragmentation of Golgi cisternae in mitotic prophase (Acharya et al. 1998, Jesch et al. 2001, Colanzi et al. 2003, Shaul and Seger 2006, Duran et al. 2008, Feinstein and Linstedt 2007, Feinstein and Linstedt 2008, Xiang and Wang 2010).

**Literature references**


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Phosphorylation of GORASP1, GOLGA2 and RAB1A by CDK1:CCNB

Location: Golgi Cisternae Pericentriolar Stack Reorganization

Stable identifier: R-HSA-2172183

Type: transition

Compartments: Golgi membrane, cytosol

Inferred from: Phosphorylation of Gorasp1, Golga2 and RAB1A by CDK1:CCNB (Homo sapiens)

GORASP1 (GRASP65) and GOLGA2 (GM130) form a complex on cis-Golgi membranes. RAB1A or RAB1B, small RAS GTP-ases, can also associate with this complex through interaction with GOLGA2 (Moyer et al. 2001, Weide et al. 2001). GOLGA2 provides a docking site for the USO1 (p115) homodimer (Nakamura et al. 1995, Seeman et al. 2000). RAB1 also participates in this interaction and facilitates it when in the GTP-bound state (Moyer et al. 2001). Binding of USO1 to GORASP1:GOLGA2:RAB1:GTP complex enables fusion of vesicles originating in the endoplasmic reticulum (ER) with cisternae of cis-Golgi.

In mitotic prophase, CDK1 (CDC2) in complex with either CCNB1 (cyclin B1) or CCNB2 (cyclin B2), as both CCNB1 and CCNB2 can localize to Golgi (Jackman et al. 1995, Draviam et al. 2001), phosphorylates GORASP1, GOLGA2 and RAB1 (Bailly et al. 1991, Lowe et al. 1998, Preisinger et al. 2005). Phosphorylation of GOLGA2 and RAB1 impairs their association with USO1, which inhibits tethering and subsequent fusion of ER-originating vesicles with cis-Golgi cisternae, resulting in cessation of ER to Golgi protein trafficking at the start of mitosis and increase in the number of Golgi trafficking vesicles at the expense of Golgi cisternae (Lowe et al. 1998, Seeman et al. 2000, Moyer et al. 2001, Diao et al. 2008).

Followed by: GOLGA2 phosphorylated by CDK1 is unable to promote fusion of ER to Golgi transport vesicles with cis-Golgi, Recruitment of PLK1 to phosphorylated GORASP1 (GRASP65)

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GOLGA2 phosphorylated by CDK1 is unable to promote fusion of ER to Golgi transport vesicles with cis-Golgi

Location: Golgi Cisternae Pericentriolar Stack Reorganization

Stable identifier: R-HSA-2314569

Type: omitted

Compartments: Golgi membrane, ER to Golgi transport vesicle membrane

USO1 (p115) protein, localizing to membranes of ER to Golgi transport vesicles, binds GOLGA2 (GM130), localizing to membranes of cis-Golgi cisternae. Binding of USO1 to GOLGA2 enables tethering of ER to Golgi transport vesicles to cis-Golgi cisternae, and is facilitated by a Ras-related GTPase RAB1. Fusion of ER to Golgi transport vesicles with cis-Golgi succeeds tethering and depends on STX5 (syntaxin-5). In mitosis, phosphorylation of GOLGA2 by cyclin B-activated CDK1 prevents USO1 docking. This results in cessation of ER to Golgi transport. Halting ER to Golgi transport increases the number of transport vesicles at the expense of Golgi cisternae, since transport vesicles keep budding from the ER but are unable to fuse with Golgi cisternae and deliver their content (Lowe et al. 1998, Seeman et al. 2000, Diao et al. 2008).

Preceded by: Phosphorylation of GORASP1, GOLGA2 and RAB1A by CDK1:CCNB

Literature references


Recruitment of PLK1 to phosphorylated GORASP1 (GRASP65)

Location: Golgi Cisternae Pericentriolar Stack Reorganization

Stable identifier: R-HSA-2172194

Type: binding

Compartments: Golgi membrane, cytosol

Inferred from: PLK1 binds phosphorylated Gorasp1 (Homo sapiens)

Phosphorylation of GORASP1 (GRASP65) by cyclin B-associated CDK1 creates a docking site for PLK1. PLK1 is also able to bind to CDK1-phosphorylated RAB1, but not to CDK1-phosphorylated GOLGA2 (Preisinger et al. 2005).

Preceded by: Phosphorylation of GORASP1, GOLGA2 and RAB1A by CDK1:CCNB

Followed by: PLK1 phosphorylates GORASP1

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**PLK1 phosphorylates GORASP1**

**Location:** Golgi Cisternae Pericentriolar Stack Reorganization

**Stable identifier:** R-HSA-2214351

**Type:** transition

**Compartments:** Golgi membrane, cytosol

CDK1-mediated phosphorylation of GORASP1 (GRASP65) enables GORASP1 to recruit PLK1 (Preisinger et al. 2005). PLK1 phosphorylates GORASP1 on serine residue S189 (Sengupta and Linstedt 2010). This serine residue is near the GORASP1 region involved in GORASP1 dimerization and oligomerization, a process underlying the stacking of cis-Golgi cisternae (Wang et al. 2003). The phosphorylation of S189 by PLK1 impairs Golgi cisternae stacking (tethering), contributing to Golgi unlinking and fragmentation in mitosis, probably by preventing formation of GORASP1 dimers and oligomers (Sutterlin et al. 2001, Sengupta and Linstedt, 2010). Two other potential phosphorylation sites that match PLK1 substrate consensus sequence exist in GORASP1, but their functional significance has not yet been examined (Sengupta and Linstedt, 2010).

**Preceded by:** Recruitment of PLK1 to phosphorylated GORASP1 (GRASP65)

**Followed by:** GORASP1 phosphorylated by PLK1 and GORASP2 phosphorylated by MAPK3-3/MAPK1 are unable to promote Golgi cisternae stacking

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GORASP2 (GRASP55) localizes to the median region of Golgi, where it forms a complex with BLZF1 (Golgin 45) and RAB2A GTPase (Short et al. 2001). Similar to GORASP1, GORASP2 is involved in the maintenance of Golgi structure and positively regulates stacking of Golgi cisternae (Xiang and Wang 2010). In addition, GORASP2, probably through its association with RAB2A GTPase, regulates trafficking through the Golgi (Short et al. 2001). In G2 and mitotic prophase, GORASP2 is phosphorylated by MEK1/2 activated MAP kinases. Monophosphorylated MAPK3 (ERK1) isoform, MAPK3 3 i.e. ERK1b (known as ERK1c in rat), likely activated by a MEK1 isoform MEK1b (Shaul et al. 2009), as well as MAPK1 (ERK2) are implicated in GORASP2 phosphorylation during mitosis (Jesch et al. 2001, Colanzi et al. 2003, Shaul and Seger 2006, Feinstein and Linstedt 2007, Duran et al. 2008, Feinstein and Linstedt 2008). Threonine residues T222 and T225 were implicated as targets of MAPK mediated GORASP2 phosphorylation in studies that used directional mutagenesis (Jesch et al. 2001, Feinstein and Linstedt 2008). However both T222 and T225 were simultaneously mutated in these studies and their roles have not been individually investigated. Using mass spectroscopy, T225 but not T222 was identified as a GORASP2 residue phosphorylated by mitotic cytosol (Duran et al. 2008). T249 residue of GORASP2 was also phosphorylated by mitotic cytosol, but the involvement of ERKs in T249 phosphorylation has not been examined (Duran et al. 2008).

Followed by: GORASP1 phosphorylated by PLK1 and GORASP2 phosphorylated by MAPK3-3/MAPK1 are unable to promote Golgi cisternae stacking

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GORASP1 phosphorylated by PLK1 and GORASP2 phosphorylated by MAPK3-3/MAPK1 are unable to promote Golgi cisternae stacking

**Location:** Golgi Cisternae Pericentriolar Stack Reorganization

**Stable identifier:** R-HSA-2314566

**Type:** omitted

**Compartments:** Golgi membrane

Adjacent cisternae of the Golgi apparatus are stacked and linked by tubules to from a Golgi ribbon (Nakamura et al. 2012). GORASP1 (GRASP65), a protein localizing to membranes of cis-Golgi cisternae, enables stacking by in trans dimerization/oligomerization through its PDZ domains (Tang et al. 2010). In mitosis, GORASP1 is phosphorylated by CDK1 and PLK1 (Preisinger et al. 2005). PLK1-mediated phosphorylation of GORASP1 prevents stacking of Golgi cisternae and contributes to unlinking and fragmentation of the Golgi apparatus, probably by interfering with GORASP1 oligomerization (Wang et al. 2003, Sengupta and Linstedt 2010). Similarly, GORASP2 (GRASP55), localized to median Golgi cisternae, promotes stacking by trans-oligomerization. Trans-oligomerization of GORASP2 is prevented by mitotic phosphorylation of GORASP2 downstream of MEK/ERK cascade, and contributes to the Golgi fragmentation in prophase (Xiang and Wang 2010).

**Preceded by:** PLK1 phosphorylates GORASP1, MAPK3-3 or MAPK1 phosphorylate GORASP2

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