



## 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. [↗](#)

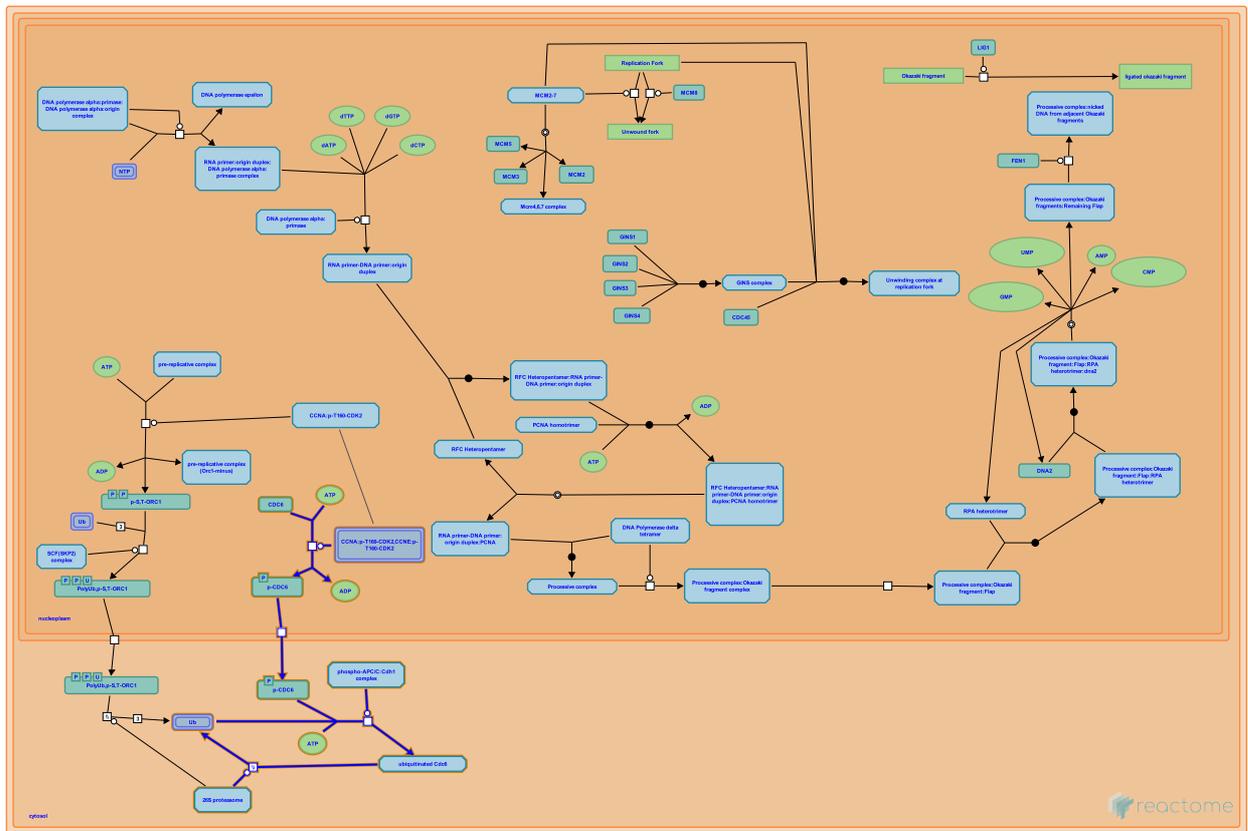
Reactome database release: 75

This document contains 1 pathway and 4 reactions ([see Table of Contents](#))

# CDK-mediated phosphorylation and removal of Cdc6 ↗

Stable identifier: R-HSA-69017

Compartments: nucleoplasm, cytosol



As cells enter S phase, HsCdc6p is phosphorylated by CDK promoting its export from the nucleus (see Bell and Dutta 2002).

## Literature references

Bell, SP., Dutta, A. (2002). DNA replication in eukaryotic cells. *Annu Rev Biochem*, 71, 333-74. ↗

Mendez, J., Stillman, B. (2000). Chromatin association of human origin recognition complex, cdc6, and minichromosome maintenance proteins during the cell cycle: assembly of prereplication complexes in late mitosis. *Mol Cell Biol*, 20, 8602-12. ↗

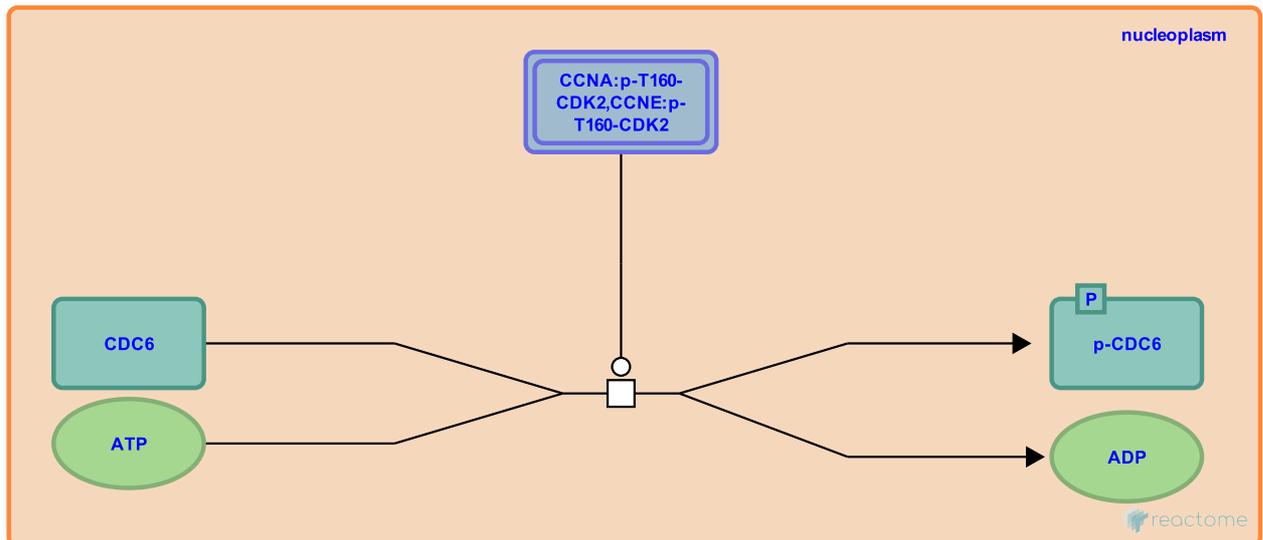
## Cdc6 protein is phosphorylated by CDK [↗](#)

**Location:** [CDK-mediated phosphorylation and removal of Cdc6](#)

**Stable identifier:** R-HSA-69005

**Type:** transition

**Compartments:** nucleoplasm



At the beginning of this reaction, 1 molecule of 'CDC6', and 1 molecule of 'ATP' are present. At the end of this reaction, 1 molecule of 'ADP', and 1 molecule of 'phosphorylated Cdc6' are present.

This reaction takes place in the 'nucleus' and is mediated by the 'kinase activity' of 'CDK'.

**Followed by:** [Phosphorylated Cdc6 is exported from the nucleus](#)

### Literature references

Jiang, W., Wells, NJ., Hunter, T. (1999). Multistep regulation of DNA replication by Cdk phosphorylation of HsCdc6. *Proc Natl Acad Sci U S A*, 96, 6193-8. [↗](#)

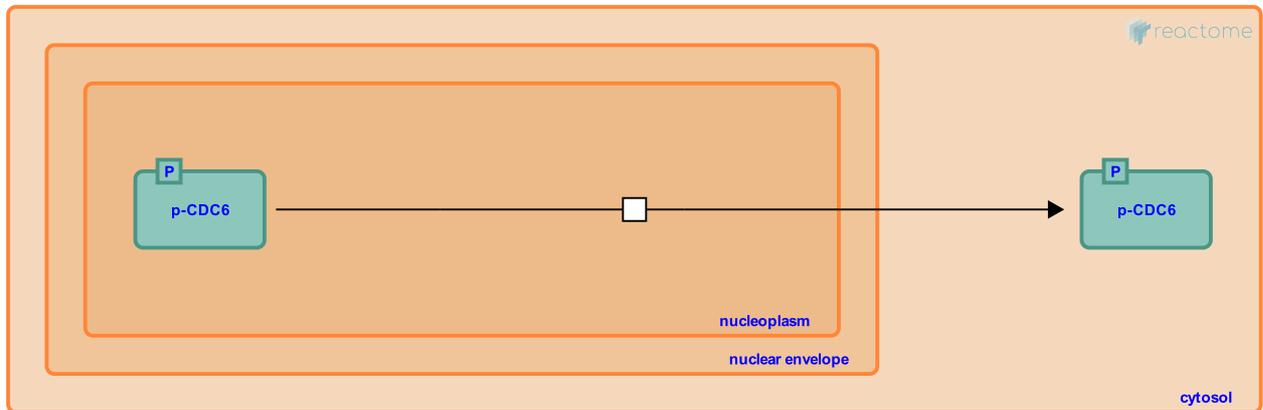
## Phosphorylated Cdc6 is exported from the nucleus ↗

**Location:** CDK-mediated phosphorylation and removal of Cdc6

**Stable identifier:** R-HSA-69006

**Type:** transition

**Compartments:** nucleoplasm, cytosol



In this reaction, 1 molecule of 'phosphorylated Cdc6' is translocated from nucleoplasm to cytosol.

This movement of the molecule occurs through the 'nuclear pore'.

**Preceded by:** Cdc6 protein is phosphorylated by CDK

**Followed by:** Cytoplasmic phosphorylated Cdc6 is ubiquitinated by the anaphase-promoting complex

### Literature references

Jiang, W., Wells, N.J., Hunter, T. (1999). Multistep regulation of DNA replication by Cdk phosphorylation of HsCdc6. *Proc Natl Acad Sci U S A*, 96, 6193-8. ↗

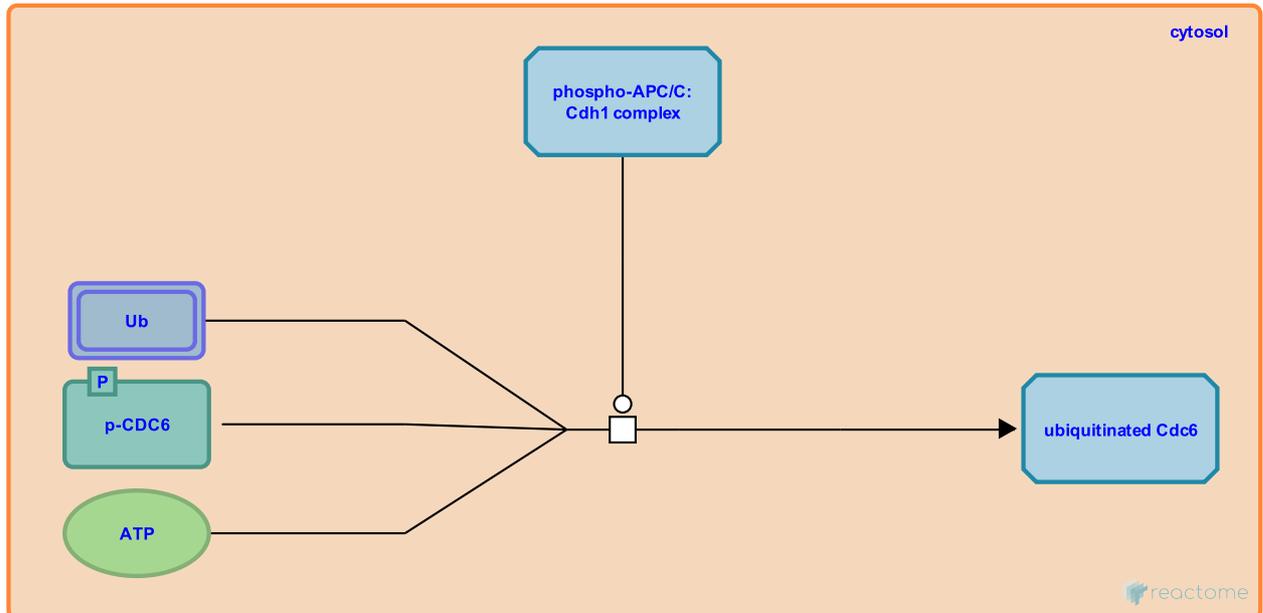
## Cytoplasmic phosphorylated Cdc6 is ubiquitinated by the anaphase-promoting complex [↗](#)

**Location:** [CDK-mediated phosphorylation and removal of Cdc6](#)

**Stable identifier:** R-HSA-69015

**Type:** transition

**Compartments:** cytosol



At the beginning of this reaction, 1 molecule of 'phosphorylated Cdc6', 1 molecule of 'ubiquitin', and 1 molecule of 'ATP' are present. At the end of this reaction, 1 molecule of 'ubiquitinated Cdc6' is present.

This reaction takes place in the 'cytosol' and is mediated by the 'endopeptidase activity' of 'anaphase-promoting complex (APC)'.

**Preceded by:** [Phosphorylated Cdc6 is exported from the nucleus](#)

**Followed by:** [Ubiquitinated Cdc6 is degraded by the proteasome](#)

### Literature references

Petersen, BO., Wagener, C., Marinoni, F., Kramer, ER., Melixetian, M., Denchi, EL. et al. (2000). Cell cycle- and cell growth-regulated proteolysis of mammalian CDC6 is dependent on APC-CDH1. *Genes Dev*, 14, 2330-43. [↗](#)

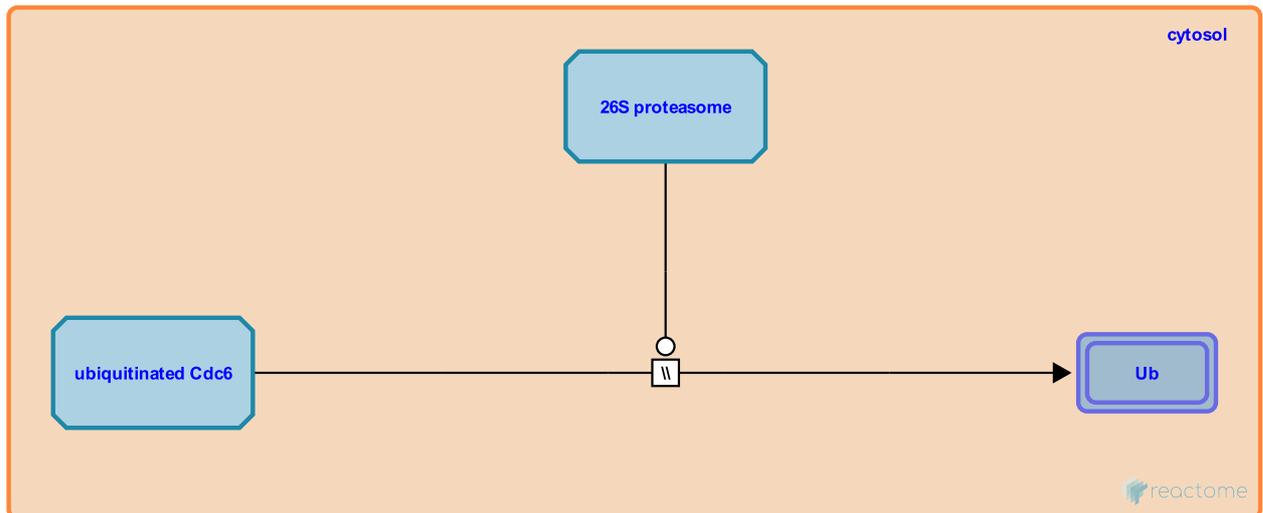
## Ubiquitinated Cdc6 is degraded by the proteasome ↗

**Location:** [CDK-mediated phosphorylation and removal of Cdc6](#)

**Stable identifier:** R-HSA-69016

**Type:** omitted

**Compartments:** cytosol



At the beginning of this reaction, 1 molecule of 'ubiquitinated Cdc6' is present. At the end of this reaction, 1 molecule of 'ubiquitin' is present.

This reaction takes place in the 'cytosol' and is mediated by the 'endopeptidase activity' of '26S proteasome'.

**Preceded by:** [Cytoplasmic phosphorylated Cdc6 is ubiquitinated by the anaphase-promoting complex](#)

### Literature references

Mendez, J., Stillman, B. (2000). Chromatin association of human origin recognition complex, cdc6, and minichromosome maintenance proteins during the cell cycle: assembly of prereplication complexes in late mitosis. *Mol Cell Biol*, 20, 8602-12. ↗

# Table of Contents

Introduction	1
☒ CDK-mediated phosphorylation and removal of Cdc6	2
↳ Cdc6 protein is phosphorylated by CDK	3
↳ Phosphorylated Cdc6 is exported from the nucleus	4
↳ Cytoplasmic phosphorylated Cdc6 is ubiquitinated by the anaphase-promoting complex	5
☒ Ubiquitinated Cdc6 is degraded by the proteasome	6
Table of Contents	7