S Phase

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

17/12/2022
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


Reactome database release: 83

This document contains 5 pathways (see Table of Contents)

https://reactome.org
DNA synthesis occurs in the S phase, or the synthesis phase, of the cell cycle. The cell duplicates its hereditary material, and two copies of the chromosome are formed. As DNA replication continues, the E type cyclins shared by the G1 and S phases, are destroyed and the levels of the mitotic cyclins rise.

**Editions**

2018-07-10  Reviewed  Manfredi, JJ.
Cyclin A:Cdk2 plays a key role in S phase entry by phosphorylation of proteins including Cdh1, Rb, p21, and p27. During G1 phase of the cell cycle, cyclin A is synthesized and associates with Cdk2. After forming in the cytoplasm, the Cyclin A:Cdk2 complexes are translocated to the nucleus (Jackman et al., 2002). Prior to S phase entry, the activity of Cyclin A:Cdk2 complexes is negatively regulated through Tyr 15 phosphorylation of Cdk2 (Gu et al., 1995) and also by the association of the cyclin kinase inhibitors (CKIs), p27 and p21. Phosphorylation of cyclin-dependent kinases (CDKs) by the CDK-activating kinase (CAK) is required for the activation of the CDK2 kinase activity (Aprelikova et al., 1995). The entry into S phase is promoted by the removal of inhibitory Tyr 15 phosphates from the Cdk2 subunit of Cyclin A:Cdk2 complex by the Cdc25 phosphatases (Blomberg and Hoffmann, 1999) and by SCF(Skp2)-mediated degradation of p27/p21 (see Ganoth et al., 2001).

While Cdk2 is thought to play a primary role in regulating entry into S phase, recent evidence indicates that Cdk1 is equally capable of promoting entry into S phase and the initiation of DNA replication (see Bashir and Pagano, 2005). Thus, Cdk1 complexes may also play a significant role at this point in the cell cycle.

**Literature references**


**Editions**

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The actual synthesis of DNA occurs in the S phase of the cell cycle. This includes the initiation of DNA replication, when the first nucleotide of the new strand is laid down during the synthesis of the primer. The DNA replication preinitiation events begin in late M or early G1 phase.
Ubiquitin-dependent degradation of Cyclin D

Location: S Phase

Stable identifier: R-HSA-75815

Cyclin D turnover is regulated by ubiquitination and proteasomal degradation which are positively regulated by cyclin D phosphorylation on threonine-286 (Diehl et al., 1997).

After the Cyclin D serves the role of mediating reactions by Cdk4 and Cdk6, it is shuttled to the cytoplasm and degraded in a ubiquitin-dependent manner. Whether Cdk4 and Cdk6 are truly redundant is a topic still under investigation, although both the kinases are required for normal cell cycle progression.

Destruction of the D type cyclins accompanies the end of the G1 phase, and the E type cyclins are involved in transition of the cell from G1 to S phase.

Literature references

Establishment of Sister Chromatid Cohesion

Location: S Phase

Stable identifier: R-HSA-2468052

Compartments: nucleoplasm, chromosome, centromeric region, chromosome

The cohesin complex loads onto chromatin in telophase, but its association with chromatin remains transient, dynamic until the S-phase of the cell cycle, presumably because the cohesin-bound NIPBL:MAU2 (SCC2:SCC4) complex promotes chromatin loading, while cohesin-bound WAPAL promotes dissociation from chromatin. Stable binding of cohesin complexes to chromatin, measured by a mean residence time on chromatin, is triggered by DNA replication in S-phase (Gerlich et al. 2006), consistent with establishment of sister chromatid cohesion.

In S-phase, acetyltransferases ESCO1 and ESCO2 acetylate the SMC3 cohesin subunit (Hou and Zou 2005, Zhang et al. 2008, Nishiyama et al. 2010, Whelan et al. 2012). The acetylation of SMC3, in addition to DNA replication and the presence of PDS5 on cohesin, facilitates the recruitment of CDCA5 (Sororin) to cohesin complexes, an essential step in the establishment of sister chromatid cohesion in mammalian cells (Rankin et al. 2005, Nishiyama et al. 2010). CDCA5 (Sororin) displaces WAPAL from PDS5, thus preventing WAPAL to interfere with the establishment of sister chromatid cohesion (Nishiyama et al. 2010). The establishment and temporal regulation of sister chromatid cohesion is necessary for equal segregation of replicated chromosomes to daughter cells.

Literature references


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