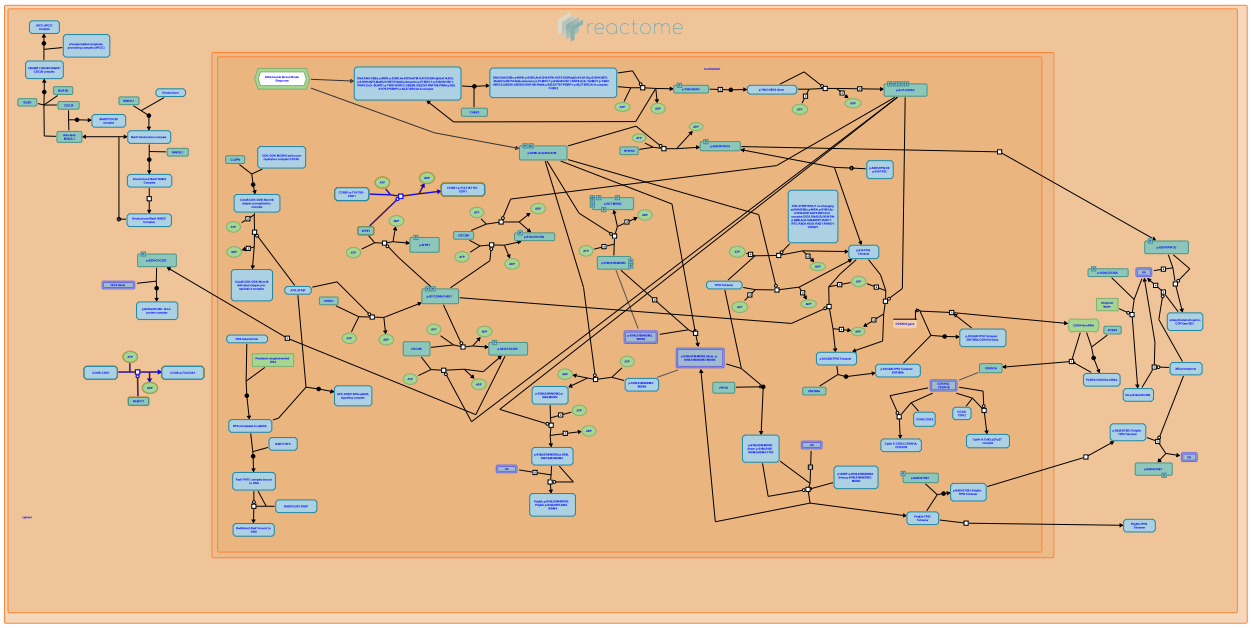
G2/M DNA replication checkpoint



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

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.

05/05/2024

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

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. ↗

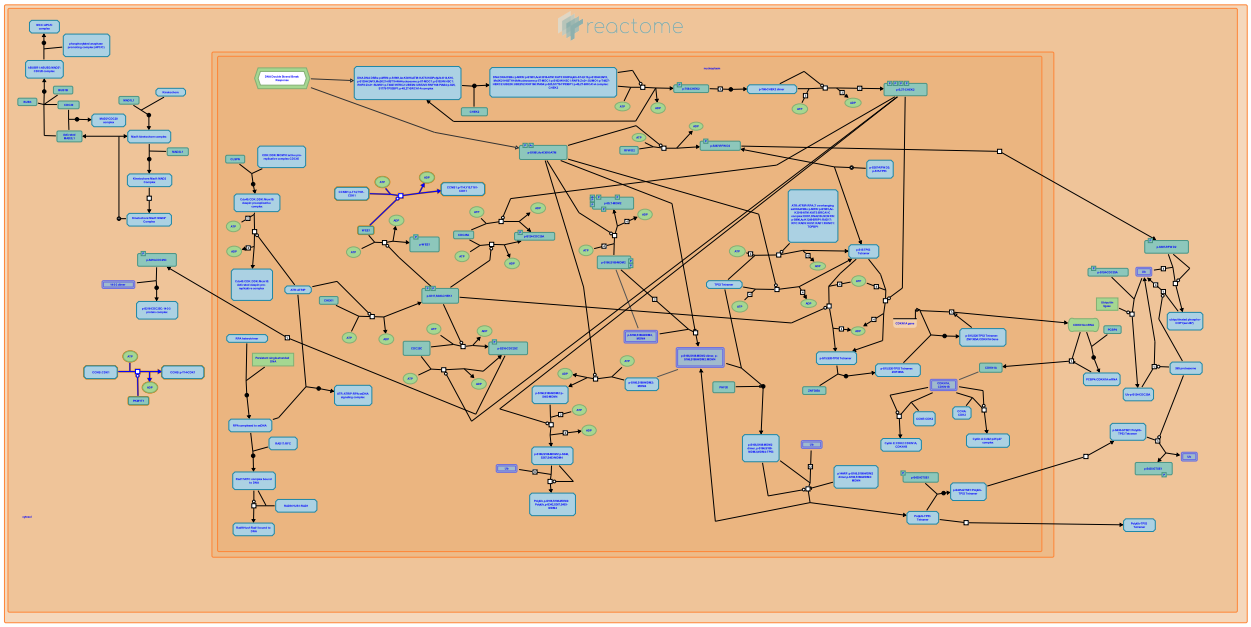
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

G2/M DNA replication checkpoint ↗

Stable identifier: R-HSA-69478



The G2/M DNA replication checkpoint ensures that mitosis is not initiated until DNA replication is complete. If replication is blocked, the DNA replication checkpoint signals to maintain Cyclin B - Cdc2 complexes in their T14Y15 phosphorylated and inactive state. This prevents the phosphorylation of proteins involved in G2/M transition, and prevents mitotic entry.

Failure of these checkpoints results in changes of ploidy: in the case of mitosis without completion of DNA replication, aneuploidy of <2C will result, and the opposite is true if DNA replication is completed more than once in a single cell cycle with an overall increase in ploidy. The mechanism by which unreplicated DNA is first detected by the cell is unknown.

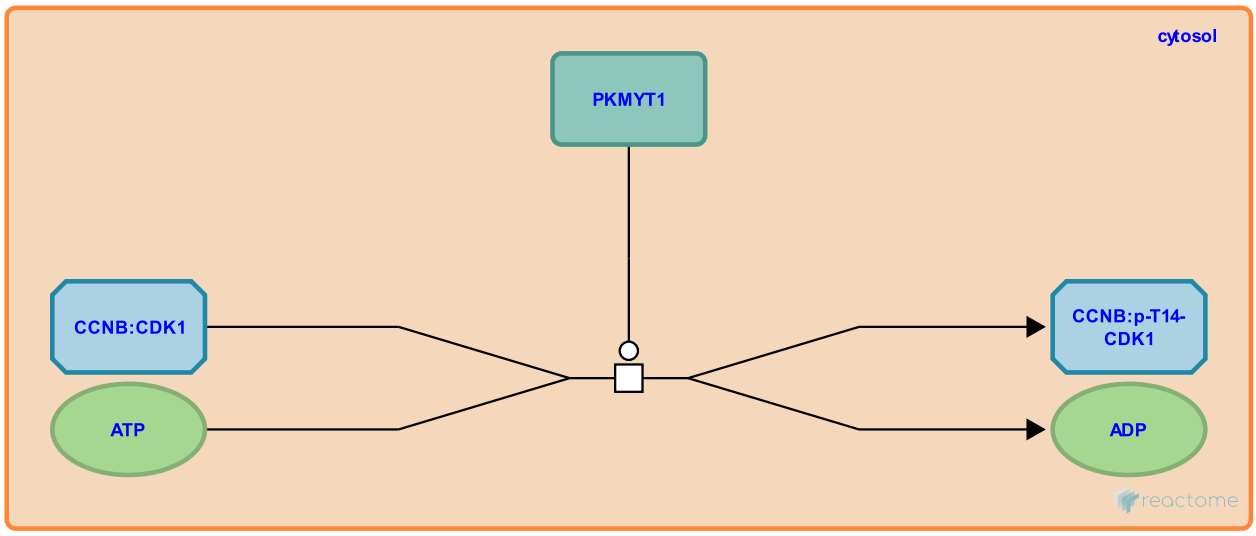
Myt-1 mediated phosphorylation of Cyclin B:Cdc2 complexes ↗

Location: G2/M DNA replication checkpoint

Stable identifier: R-HSA-170055

Type: transition

Compartments: cytosol



Myt1, which localizes preferentially to the endoplasmic reticulum and Golgi complex, phosphorylates Cdc2 on threonine 14 (Liu et al., 1997).

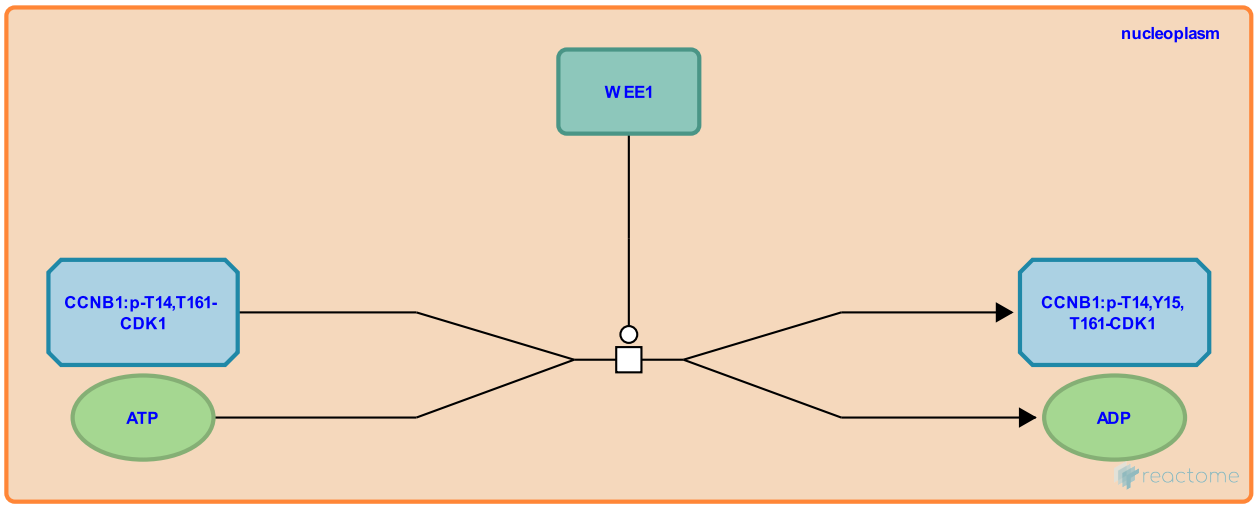
Wee1-mediated phosphorylation of Cyclin B1:phospho-Cdc2 complexes ↗

Location: G2/M DNA replication checkpoint

Stable identifier: R-HSA-170070

Type: transition

Compartments: nucleoplasm



WEE1, a nuclear kinase, phosphorylates cyclin B1:Cdc2 (CCNB1:CDK1) on tyrosine 15 (Y15), inactivating the complex (Parker and Piwnica-Worms 1992, McGowan and Russell 1993). The complex of cyclin B2 and Cdc2 (CCNB2:CDK1) is also phosphorylated on Y15 (Galaktionov and Beach 1991).

Literature references

Galaktionov, K., Beach, D. (1991). Specific activation of cdc25 tyrosine phosphatases by B-type cyclins: evidence for multiple roles of mitotic cyclins. *Cell, 67*, 1181-94. ↗

Piwnica-Worms, H., Parker, LL. (1992). Inactivation of the p34cdc2-cyclin B complex by the human WEE1 tyrosine kinase. *Science, 257*, 1955-7. ↗

McGowan, CH., Russell, P. (1993). Human Wee1 kinase inhibits cell division by phosphorylating p34cdc2 exclusively on Tyr15. *EMBO J., 12*, 75-85. ↗

Table of Contents