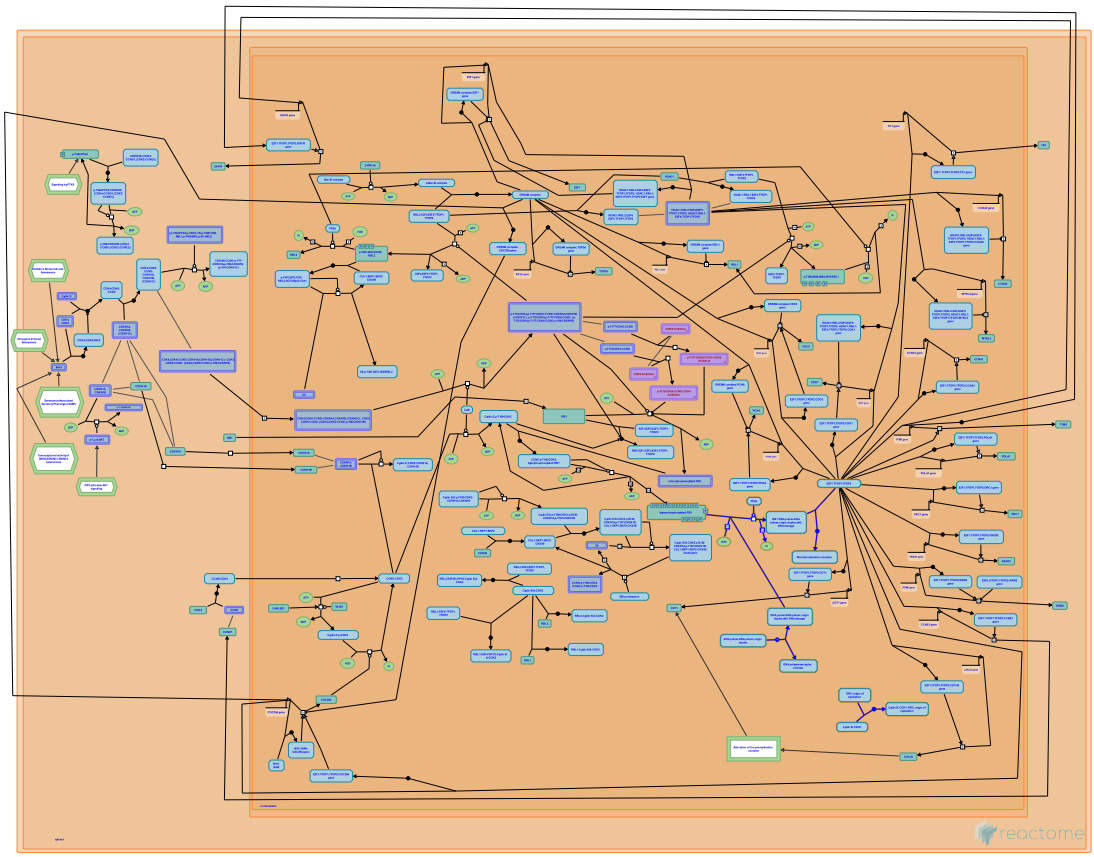
E2F mediated regulation of DNA replication



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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.

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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. ↗

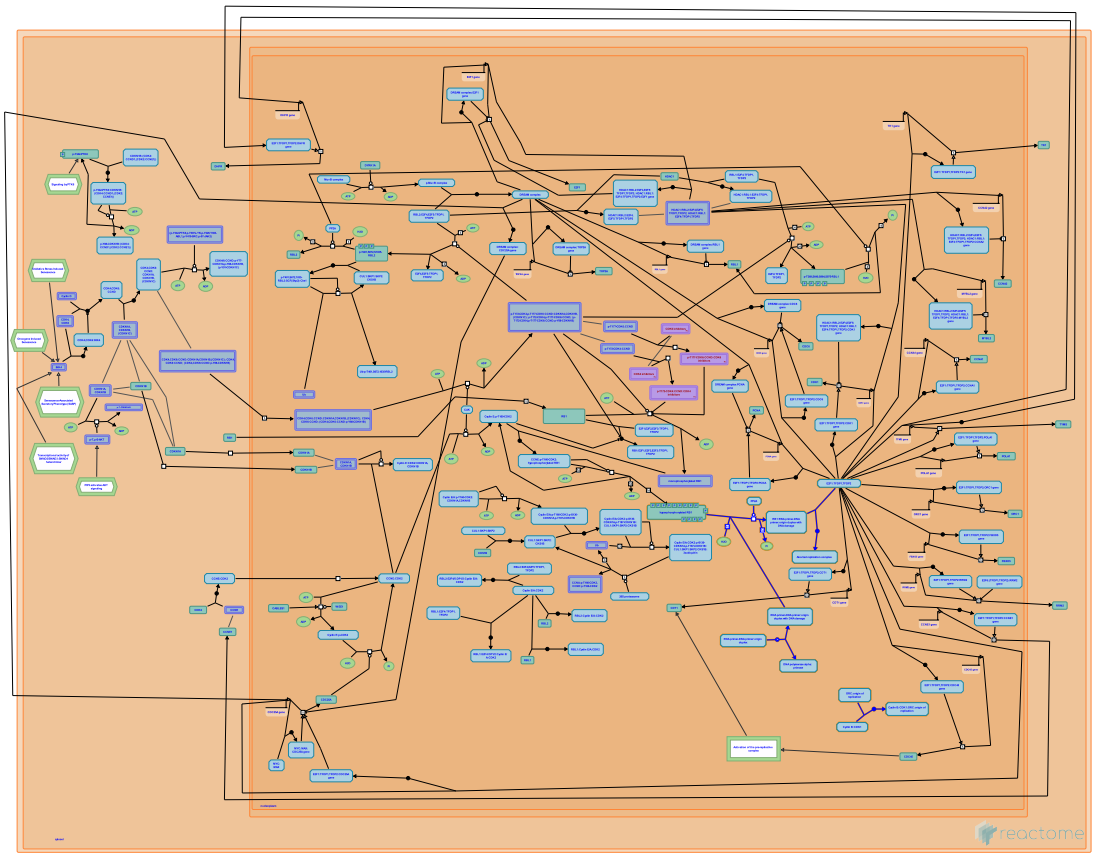
Reactome database release: 90

This document contains 3 pathways (see Table of Contents)

E2F mediated regulation of DNA replication ↗

Stable identifier: R-HSA-113510

Compartments: nucleoplasm



Progression through G1 and G1 to S-phase transition that initiates DNA synthesis involve many complexes that are regulated by RB1:E2F pathway. RB1:E2F pathway plays a key role in gene expression regulation in proliferating and differentiated cells. As a repressor, E2F remains bound to RB1; it can activate the expression of S-phase genes involved in DNA replication after the phosphorylation of RB1.
E2F proteins regulate expression of genes involved in various processes thereby forming interlinks between cell cycle, DNA synthesis, DNA damage recognition etc.
In this module, activation of replication related genes by E2F1 and two ways by which E2F1 regulates DNA replication initiation are annotated.

Literature references

Castellano, MM., del Pozo, JC., Gutierrez, C., Ramirez-Parra, E. (2002). G(1) to S transition: more than a cell cycle engine switch. *Curr Opin Plant Biol, 5*, 480-6. ↗

Cam, H., Dynlacht, BD. (2003). Emerging roles for E2F: beyond the G1/S transition and DNA replication. *Cancer Cell, 3*, 311-6. ↗

Stevaux, O., Dyson, NJ. (2002). A revised picture of the E2F transcriptional network and RB function. *Curr Opin Cell Biol, 14*, 684-91. ↗

Editions

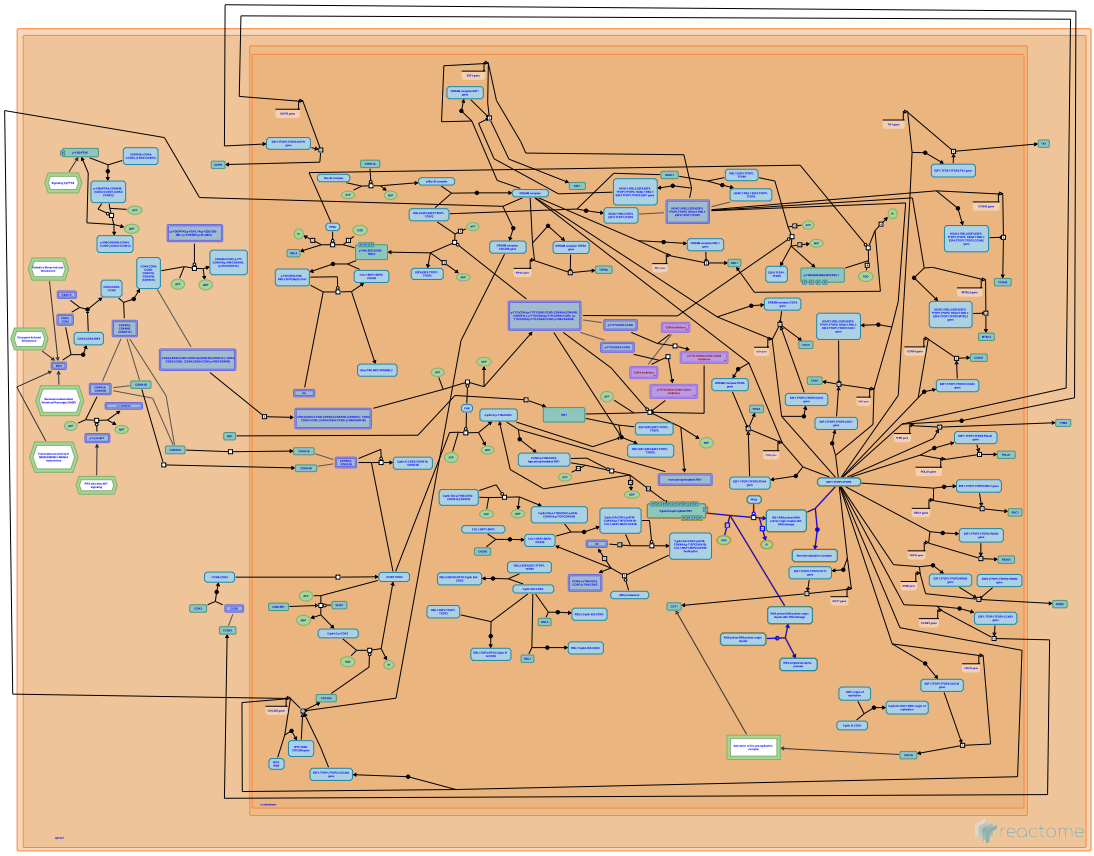
2004-06-16	Authored	Gopinathrao, G.

Inhibition of replication initiation of damaged DNA by RB1/E2F1 ↗

Location: E2F mediated regulation of DNA replication

Stable identifier: R-HSA-113501

Compartments: nucleoplasm



During S phase of the cell cycle, RB1 is dephosphorylated by the PP2A protein phosphatase complex. Unphosphorylated RB1 associates with DNA damage sites in S phase, preventing initiation of DNA replication from these sites (Knudsen et al. 2000, Avni et al. 2003).

Literature references

Livingston, DM., Ganesan, S., Scully, R., Hofmann, F., ElShamy, WM., Yang, H. et al. (2003). Active localization of the retinoblastoma protein in chromatin and its response to S phase DNA damage. *Mol Cell, 12*, 735-46. ↗

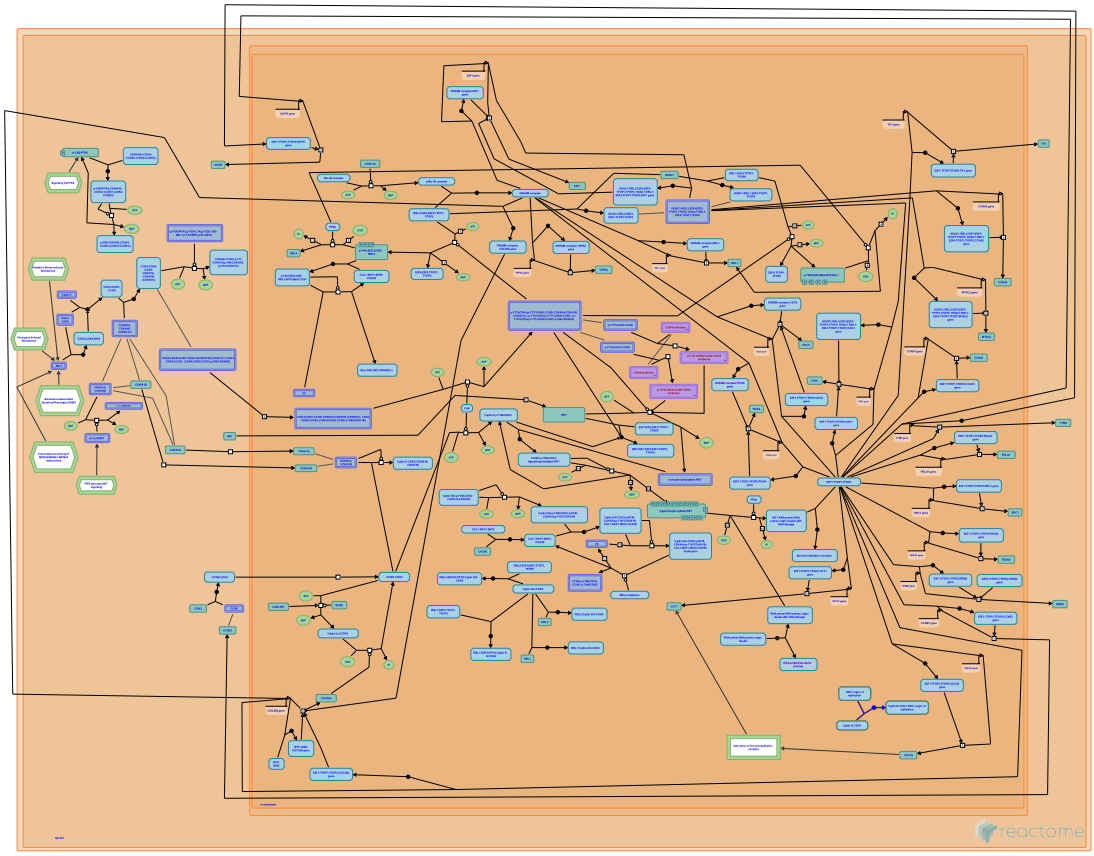
Capogrossi, MC., Martelli, F., Fasanaro, P., Di Stefano, V., Romani, S., Magenta, A. (2008). Protein phosphatase 2A subunit PR70 interacts with pRb and mediates its dephosphorylation. *Mol Cell Biol, 28*, 873-82. ↗

E2F-enabled inhibition of pre-replication complex formation ↗

Location: E2F mediated regulation of DNA replication

Stable identifier: R-HSA-113507

Compartments: nucleoplasm



Under specific conditions, Cyclin B, a mitotic cyclin, can inhibit the functions of pre-replicative complex. E2F1 activates Cdc25A protein which regulates Cyclin B in a positive manner. Cyclin B/Cdk1 function is restored which leads to the disruption of pre-replicative complex. This phenomenon has been demonstrated by Bosco et al (2001) in Drosophila.

Literature references

Kennedy, BK., Barbie, DA., Classon, M., Dyson, NJ., Harlow, E. (2000). Nuclear organization of DNA replication in primary mammalian cells. *Genes Dev, 14*, 2855-68. ↗

Editions

2004-05-26	Authored	Gopinathrao, G.

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