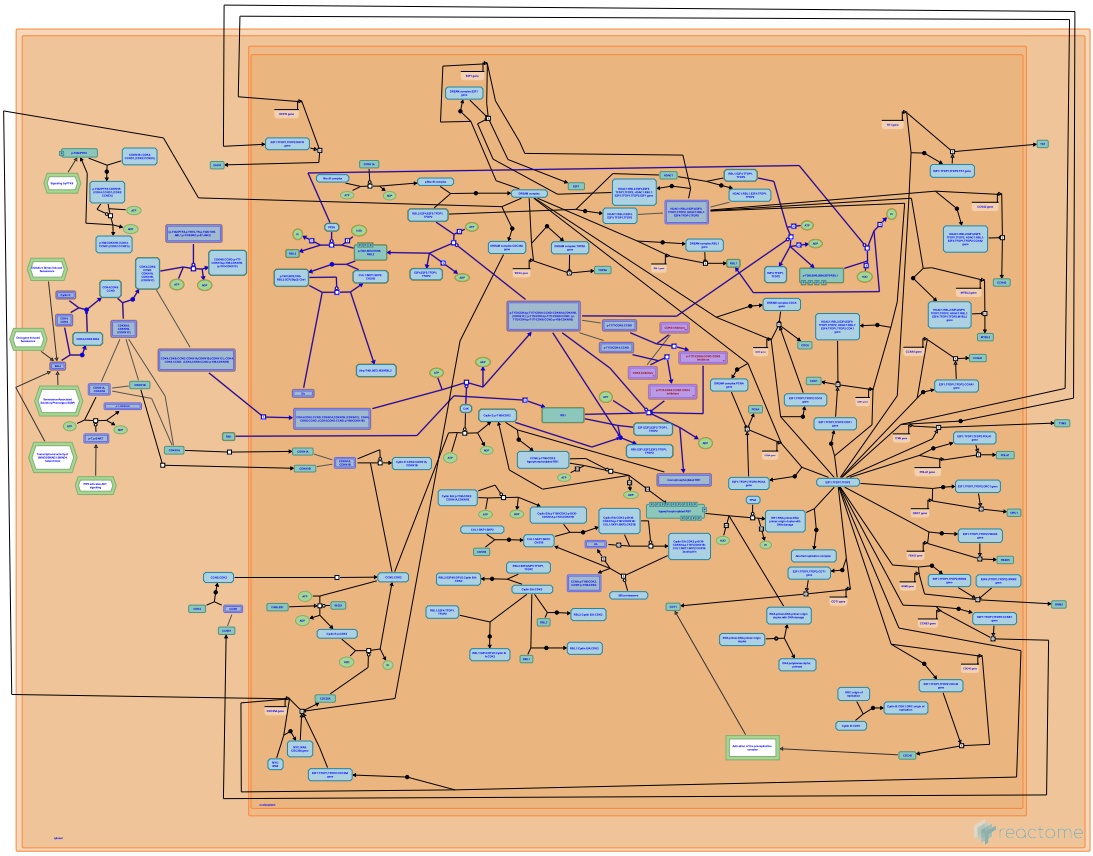
G1 Phase



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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.

26/04/2024

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

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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. ↗

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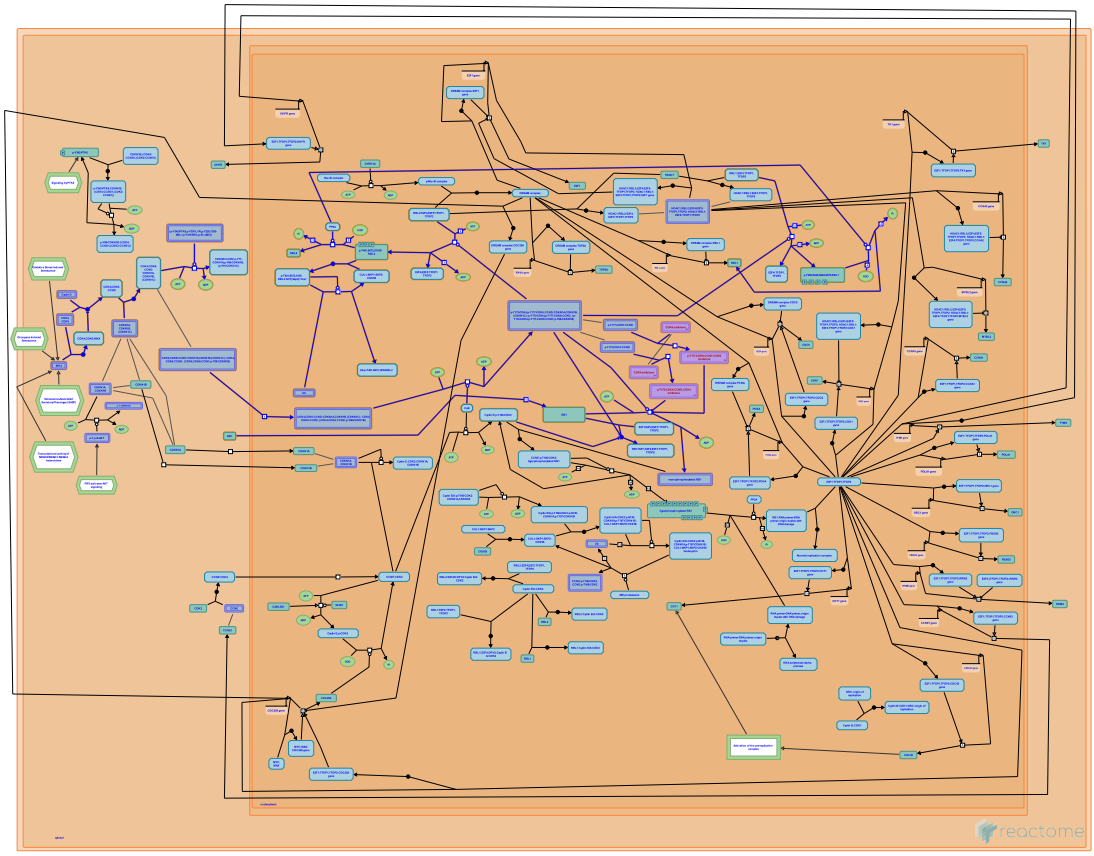
Reactome database release: 88

This document contains 2 pathways (see Table of Contents)

G1 Phase ↗

Stable identifier: R-HSA-69236

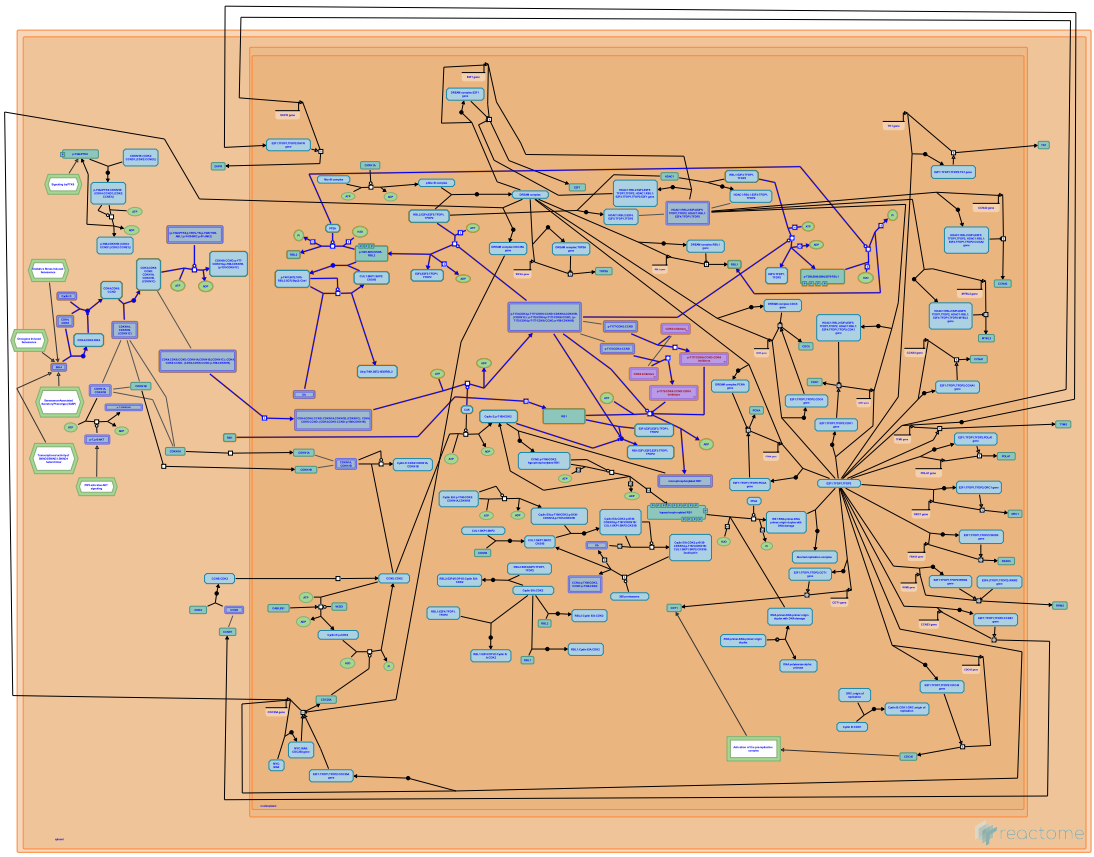


Early cell cycle progression in G1 is under the control of the D-type cyclins together with Cdk4 and Cdk6. An important target for these CDKs is the Retinoblastoma (Rb) protein, which when phosphorylated promotes cell cycle progression by releasing E2F transcription factors that transactivate several important genes for later cell cycle events. The formation of Cyclin D - Cdk4/6 complexes is promoted by two proteins, p21Cip1/Waf1 and p27kip1, and their activity can be inhibited by the binding of several small CDK-inhibitory proteins (CKIs): p15INK4B, p16INK4A, p18INK4C and p19INK4D.

Cyclin D associated events in G1 ↗

Location: G1 Phase

Stable identifier: R-HSA-69231



Three D-type cyclins are essential for progression from G1 to S-phase. These D cyclins bind to and activate both CDK4 and CDK6. The formation of all possible complexes between the D-type cyclins and CDK4/6 is promoted by the proteins, p21(CIP1/WAF1) and p27(KIP1). The cyclin-dependent kinases are then activated due to phosphorylation by CAK. The cyclin dependent kinases phosphorylate the RB1 protein and RB1-related proteins p107 (RBL1) and p130 (RBL2). Phosphorylation of RB1 leads to release of activating E2F transcription factors (E2F1, E2F2 and E2F3). After repressor E2Fs (E2F4 and E2F5) dissociate from phosphorylated RBL1 and RBL2, activating E2Fs bind to E2F promoter sites, stimulating transcription of cell cycle genes, which then results in proper G1/S transition. The binding and sequestration of p27Kip may also contribute to the activation of CDK2 cyclin E/CDK2 cyclin A complexes at the G1/S transition (Yew et al., 2001).

Editions

2016-11-04	Revised	Roger, PP.
2016-12-01	Edited	Orlic-Milacic, M.

Table of Contents