

CDKN1A (p21) prevents association of Cyclin A:Cdk2 with Cdh1

D'Eustachio, P., Matthews, L., Orlic-Milacic, M., Samarajiwa, S.

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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of [Creative Commons Attribution 4.0 International \(CC BY 4.0\) License](#). For more information see our [license](#).

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: 70

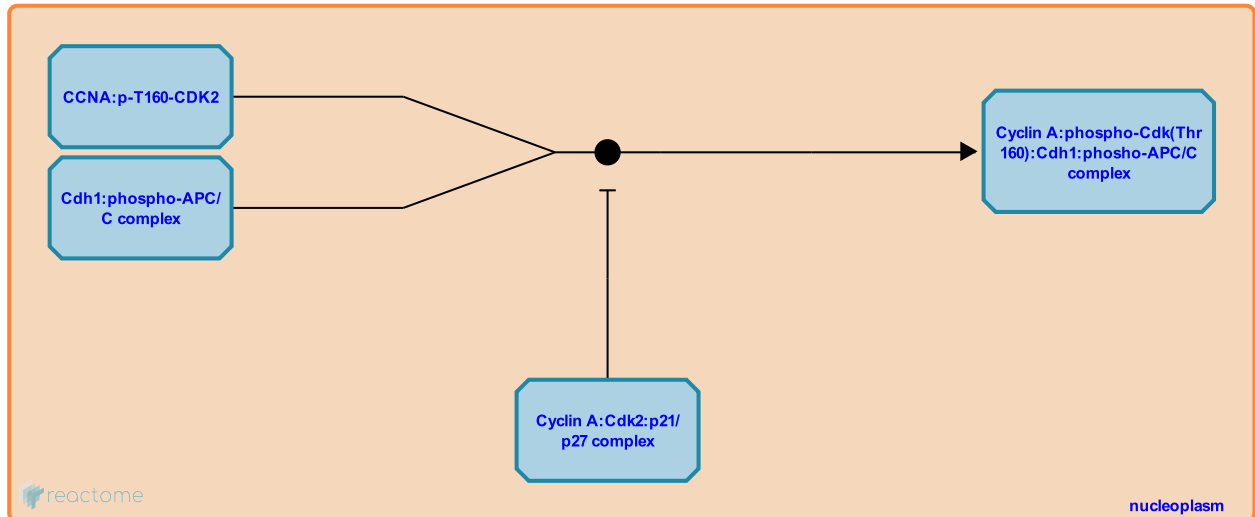
This document contains 1 reaction ([see Table of Contents](#))

CDKN1A (p21) prevents association of Cyclin A:Cdk2 with Cdh1 ↗

Stable identifier: R-HSA-3788708

Type: binding

Compartments: nucleoplasm



Cyclin A-Cdk2 (CCNA:CDK2) prevents unscheduled APC reactivation during S phase by binding and subsequently phosphorylating FZR1 (Cdh1). Phosphorylation-dependent dissociation of the Cdh1-activating subunit inhibits the APC/C (Sorensen et al. 2001). DNA damage activates ATM kinase, resulting in TP53-mediated induction of CDKN1A (p21) expression. CDKN1A binds CCNA:CDK2 complex and prevents its association with Cdh1 (Takahashi et al. 2012).

Literature references

Sorensen, CS., Lukas, C., Kramer, ER., Peters, JM., Lukas, J. (2001). A conserved cyclin-binding domain determines functional interplay between anaphase-promoting complex-Cdh1 and cyclin A-Cdk2 during cell cycle progression. *Mol Cell Biol*, 21, 3692-703. ↗

Takahashi, A., Imai, Y., Yamakoshi, K., Kuninaka, S., Ohtani, N., Yoshimoto, S. et al. (2012). DNA damage signaling triggers degradation of histone methyltransferases through APC/C(Cdh1) in senescent cells. *Mol. Cell*, 45, 123-31. ↗

Editions

2013-07-15	Edited	Matthews, L., D'Eustachio, P.
2013-07-15	Authored	Orlic-Milacic, M.
2013-09-03	Reviewed	Samarajiwa, S.