Defective RB1 does not bind

E2F1,(E2F2,E2F3)

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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

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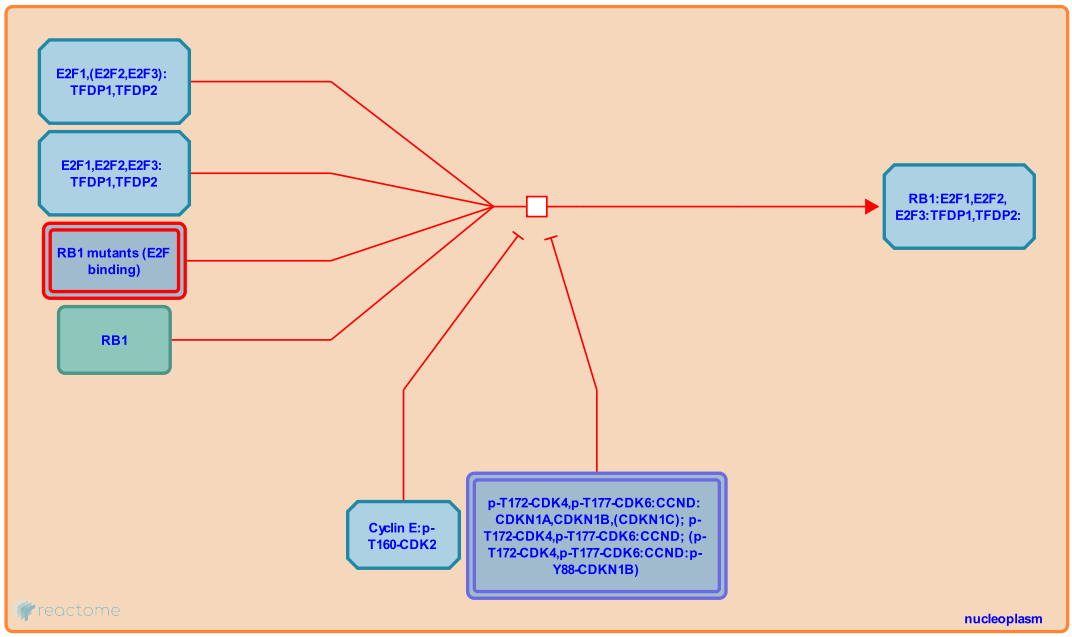
Stable identifier: R-HSA-9659782

Type: transition

Compartments: nucleoplasm

Diseases: cancer



Low penetrance germline RB1 mutants RB1 N480del and RB1 R661W, reported in retinoblastoma, localize to the nucleus but have >95% reduced binding to E2F1. These two mutations lie in the pocket region of RB1, N480del in the pocket domain A (amino acid residues 373 579) and R661W in the pocket domain B (amino acid residues 640 771). Binding of RB1 N480del and RB1 R661W to E2F2 and E2F3 has not been tested but is assumed to be affected like E2F1 binding (Otterson et al. 1997). RB1 T738_R775del mutant (also known as RB1 delEx22) is a cancer mutant that is generated by an in-frame deletion or by a splice site mutation, which both result in a mutant protein that lacks the amino acid sequence encoded by exon 22 of the RB1 gene. This mutant lacks a part of the pocket domain B and is unable to bind to the adenoviral oncoprotein E1A (Templeton et al. 1991). RB1 T738_R775del is not able to inhibit E2F1-mediate transcriptional transactivation (Helin et al. 1993) and is unable to bind to E2Fs (Ji et al. 2004).
RB1 R661Q mutant has been reported in cancer and is predicted to be pathogenic, but has not been functionally tested; it is annotated as a candidate based on its similarity with RB1 R661W.
RB1 C706F mutant, reported in lung and breast cancer, maps to the pocket domain B and shows a complete loss of binding to E2F1 (Otterson et al. 1997). Based on its similarity with RB1 C706F, RB1 C706Y mutant, reported in lung cancer, has been annotated as a candidate.
Another in-frame deletion mutant of RB1, RB1 I703_E737del (also known as RB1 delEx21) has been reported in several different cancer types. This mutant is generated by an in-frame deletion of exon 21 and is assumed to have impaired binding to E2Fs, due to its partially deleted pocket domain B. RB1 I703_E737del is annotated as a candidate for impaired binding to E2F1, E2F2 and E2F3.

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Editions

2020-05-07	Authored	Orlic-Milacic, M.
2020-05-17	Reviewed	Dick, FA.
2020-05-18	Edited	Orlic-Milacic, M.