Defective RB1 does not form a complex with SKP2 and FZR1

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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.

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Literature references

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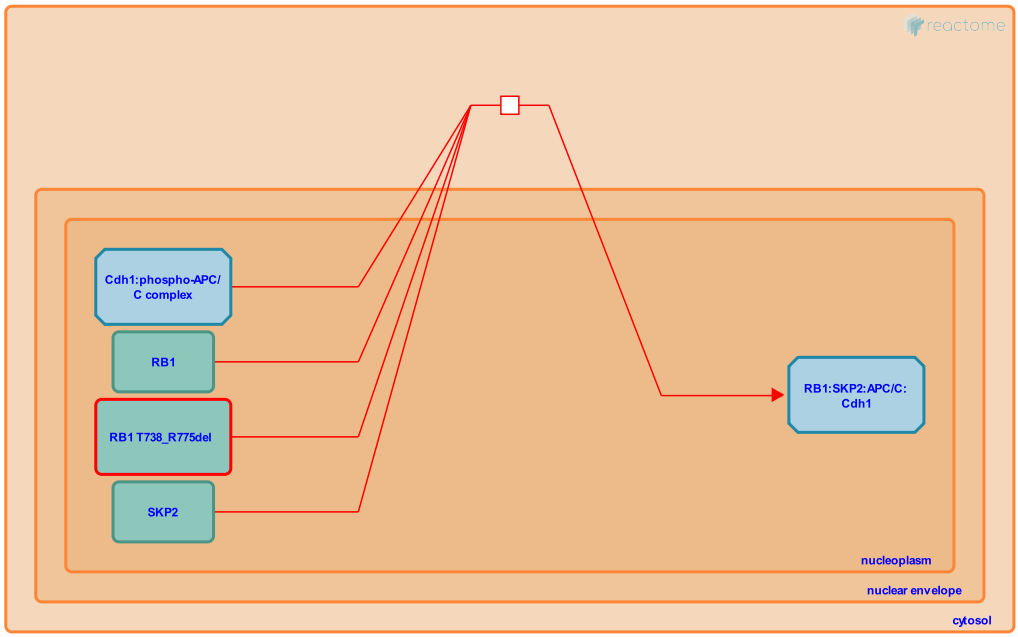
Stable identifier: R-HSA-9687377

Type: transition

Compartments: cytosol

Diseases: cancer



A tripartite complex formed between RB1, SKP2 and FZR1 (Cdh1) targets SKP2 for the anaphase promoting complex/cyclosome (APC/C:Cdh1)-mediated ubiquitination and subsequent proteasome-mediated degradation. Both SKP2 and FZR1 interact with the pocket domain of RB1, with amino acid residues 637–738 and 772–824 involved in SKP2 binding and the cleft region (amino acids 753–761), containing the LxCxE motif, involved in FZR1 binding (Binne et al. 2007). RB1 T738_R775del (RB1 Ex22del) cancer mutant, which lacks exon 22, is able to associate with SKP2 but unable to bind FZR1. This mutant is defective in inducing accumulation of CDKN1B (p27Kip1) and promoting mitotic exit as it cannot prevent SKP2-mediated ubiquitination and degradation of CDKN1B (Ji et al. 2004, Binne et al. 2007). RB1 T738_R775del mutant is also defective in E2F binding (Ji et al. 2004). RB1 missense mutant, RB1 R661W, which causes low penetrance familial retinoblastoma, is unable to bind to E2Fs but retains the ability to bind to SKP2 and FZR2 and to induce CDKN1B accumulation (Ji et al. 2004, Binne et al. 2007).

Literature references

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Editions

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