Transcriptional Regulation by E2F6

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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


E2F6, similar to other E2F proteins, possesses the DNA binding domain, the dimerization domain and the marked box. E2F6, however, does not have a pocket protein binding domain and thus does not interact with the retinoblastoma family members RB1, RBL1 (p107) and RBL2 (p130) (Gaubatz et al. 1998, Trimarchi et al. 1998). E2F6 lacks the transactivation domain and acts as a transcriptional repressor (Gaubatz et al. 1998, Trimarchi et al. 1998, Cartwright et al. 1998). E2F6 forms a heterodimer with TFDP1 (DP-1) (Trimarchi et al. 1998, Ogawa et al. 2002, Cartwright et al. 1998) or TFDP2 (DP-2) (Gaubatz et al. 1998, Trimarchi et al. 1998, Cartwright et al. 1998).

E2f6 knockout mice are viable and embryonic fibroblasts derived from these mice proliferate normally. Although E2f6 knockout mice appear healthy, they are affected by homeotic transformations of the axial skeleton, involving vertebrae and ribs. Similar skeletal defects have been reported in mice harboring mutations in polycomb genes, suggesting that E2F6 may function in recruitment of polycomb repressor complex(es) to target promoters (Storre et al. 2002).

E2F6 mediates repression of E2F responsive genes. While E2F6 was suggested to maintain G0 state in quiescent cells (Gaubatz et al. 1998, Ogawa et al. 2002), this finding has been challenged (Giangrande et al. 2004, Bertoli et al. 2013, Bertoli et al. 2016). Instead, E2F6-mediated gene repression in proliferating (non-quiescent) cells is thought to repress E2F targets involved in G1/S transition during S phase of the cell cycle. E2F6 does not affect E2F targets involved in G2/M transition (Oberley et al. 2003, Giangrande et al. 2004, Attwooll et al. 2005, Trojer et al. 2011, Bertoli et al. 2013). In the context of the E2F6.com-1 complex, E2F6 was shown to bind to promoters of E2F1, MYC, CDC25A and TK1 genes (Ogawa et al. 2002). E2F6 also binds the promoters of CDC6, RR1 (RR1), PCNA and TYMS (TS) genes (Giangrande et al. 2004), as well as the promoter of the DHFR gene (Gaubatz et al. 1998). While transcriptional repression by the E2F6.com 1 complex may be associated with histone methyltransferase activity (Ogawa et al. 2002), E2F6 can also repress transcription independently of H3K9 methylation (Oberley et al. 2003).

During S phase, E2F6 is involved in the DNA replication stress checkpoint (Bertoli et al. 2013, Bertoli et al. 2016). Under replication stress, CHEK1-mediated phosphorylation prevents association of E2F6 with...
its target promoters, allowing transcription of E2F target genes whose expression is needed for resolution of stalled replication forks and restart of DNA synthesis. Inability to induce transcription of E2F target genes (due to CHEK1 inhibition or E2F6 overexpression) leads to replication stress induced DNA damage (Bertoli et al. 2013, Bertoli et al. 2016). E2F6 represses transcription of a number of E2F targets involved in DNA synthesis and repair, such as RRM2, RAD51, BRCA1, and RBBP8 (Oberley et al. 2003, Bertoli et al. 2013).

**Literature references**


**Editions**

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E2F6 binds TFDP1

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