Regulation of TP53 Activity through Acetylation

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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


Reactome database release: 71

This document contains 2 pathways and 6 reactions (see Table of Contents)
Regulation of TP53 Activity through Acetylation

Stable identifier: R-HSA-6804758

Transcriptional activity of TP53 is positively regulated by acetylation of several of its lysine residues. BRD7 binds TP53 and promotes acetylation of TP53 lysine residue K382 by acetyltransferase EP300 (p300). Acetylation of K382 enhances TP53 binding to target promoters, including CDKN1A (p21), MDM2, SERPINE1, TIGAR, TNFRSF10C and NDRG1 (Bensaad et al. 2010, Burrows et al. 2010, Drost et al. 2010). The histone acetyltransferase KAT6A, in the presence of PML, also acetylates TP53 at K382, and, in addition, acetylates K120 of TP53. KAT6A-mediated acetylation increases transcriptional activation of CDKN1A by TP53 (Rokudai et al. 2013). Acetylation of K382 can be reversed by the action of the NuRD complex, containing the TP53-binding MTA2 subunit, resulting in inhibition of TP53 transcriptional activity (Luo et al. 2000). Acetylation of lysine K120 in the DNA binding domain of TP53 by the MYST family acetyltransferases KAT8 (hMOF) and KAT5 (TIP60) can modulate the decision between cell cycle arrest and apoptosis (Sykes et al. 2006, Tang et al. 2006). Studies with acetylation-defective knock-in mutant mice indicate that lysine acetylation in the p53 DNA binding domain acts in part by uncoupling transactivation and transrepression of gene targets, while retaining ability to modulate energy metabolism and production of reactive oxygen species (ROS) and influencing ferroptosis (Li et al. 2012, Jiang et al. 2015).

Literature references


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<tr>
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<tr>
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BRD7 binds TP53 and EP300

Location: Regulation of TP53 Activity through Acetylation

Stable identifier: R-HSA-3222093

Type: binding

Compartments: nucleoplasm