reactome

PTEN gene transcription is stimulated by TP53

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02/09/2021

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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Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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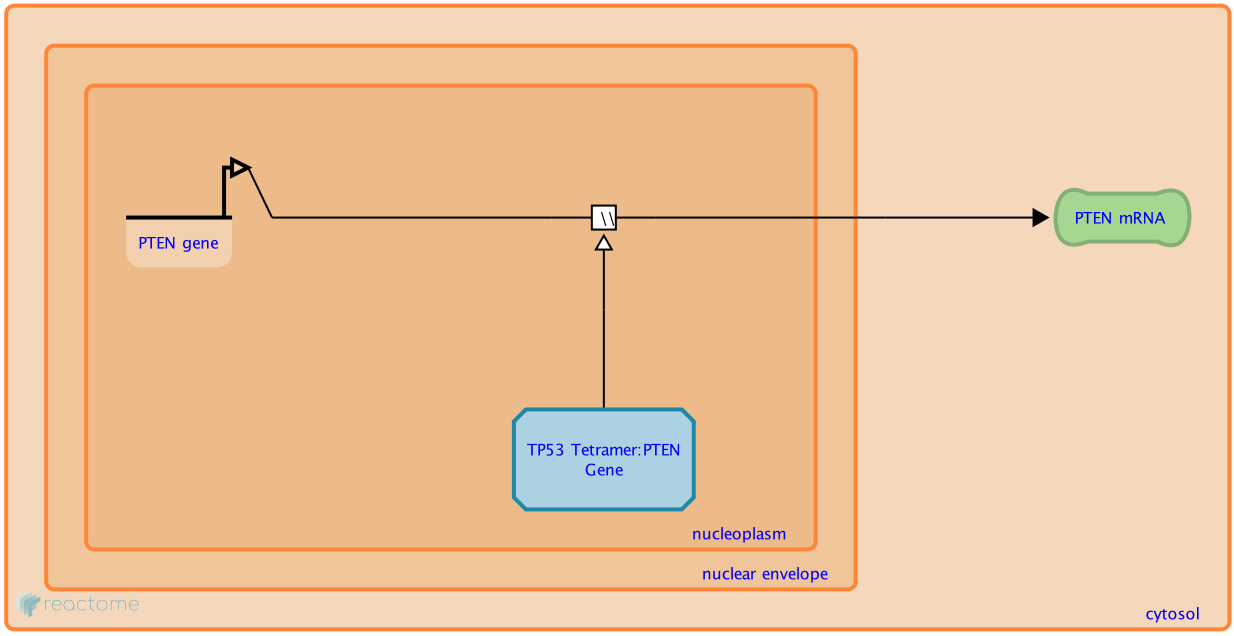
Stable identifier: R-HSA-5632993

Type: omitted

Compartments: nucleoplasm, cytosol



PTEN (phosphatase and tensin homolog deleted in chromosome 10) is a tumor suppressor gene that is deleted or mutated in a variety of human cancers. TP53 (p53) stimulates PTEN transcription (Stambolic et al. 2000, Singh et al. 2002). PTEN, acting as a negative regulator of PI3K/AKT signaling, affects cell survival, cell cycling, proliferation and migration. PTEN regulates TP53 stability by inhibiting AKT-mediated activation of TP53 ubiquitin ligase MDM2, and thus enhances TP53 transcriptional activity and its own transcriptional activation by TP53. Beside their cross-regulation, PTEN and TP53 can interact and cooperate to regulate survival or apoptotic phenomena (Stambolic et al. 2000, Singh et al. 2002, Nakanishi et al. 2014).

In response to UV induced DNA damage, PTEN transcription is stimulated by binding of the transcription factor EGR1 to the promoter region of PTEN (Virolle et al. 2001).

PTEN transcription is also stimulated by binding of the activated nuclear receptor PPARG (PPARgamma) to peroxisome proliferator response elements (PPREs) in the promoter of the PTEN gene (Patel et al. 2001), binding of the ATF2 transcription factor, activated by stress kinases of the p38 MAPK family, to ATF response elements in the PTEN gene promoter (Shen et al. 2006) and by the transcription factor MAF1 (Li et al. 2016).

NR2E1 (TLX) associated with transcription repressors binds the evolutionarily conserved TLX consensus site in the PTEN promoter. NR2E1 inhibits PTEN transcription by associating with various transcriptional repressors, probably in a cell type or tissue specific manner. PTEN transcription is inhibited when NR2E1 forms a complex with ATN1 (atrophin-1) (Zhang et al. 2006, Yokoyama et al. 2008), KDM1A (LSD1) histone methyltransferase containing CoREST complex (Yokoyama et al. 2008), or histone deacetylases HDAC3, HDAC5 or HDAC7 (Sun et al. 2007).

Binding of the transcriptional repressor SNAI1 (Snail1) to the PTEN promoter represses PTEN transcription. SNAI1-mediated repression of PTEN transcription may require phosphorylation of SNAI1 on serine residue S246. Binding of SNAI1 to the PTEN promoter increases in response to ionizing radiation and is

implicated in SNAI1-mediated resistance to gamma-radiation induced apoptosis (Escriva et al. 2008). Binding of another Slug/Snail family member SNAI2 (SLUG) to the PTEN gene promoter also represses PTEN transcription (Uygur et al. 2015).

Binding of JUN to the AP-1 element in the PTEN gene promoter (Hettinger et al. 2007) inhibits PTEN transcription. JUN partner FOS is not needed for JUN-mediated downregulation of PTEN (Vasudevan et al. 2007).

Binding of the transcription factor SALL4 to the PTEN gene promoter (Yang et al. 2008) and SALL4-medaited recruitment of the transcriptional repressor complex NuRD (Lu et al. 2009, Gao et al. 2013), containing histone deacetylases HDAC1 and HDAC2, inhibits the PTEN gene transcription. SALL4-mediated recruitment of DNA methyltransferases (DNMTs) is also implicated in transcriptional repression of PTEN (Yang et al. 2012).

Binding of the transcription factor MECOM (EVI1) to the PTEN gene promoter and MECOM-mediated recruitment of polycomb repressor complexes containing BMI1 (supposedly PRC1.4), and EZH2 (PRC2) leads to repression of PTEN transcription (Song et al. 2009, Yoshimi et al. 2011).

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Editions

2014-12-23	Authored, Edited	Orlic-Milacic, M.
2014-12-30	Reviewed	Hwang, PM., Kang, JG., Wang, PY.
2016-02-04	Reviewed	Inga, A.
2016-02-04	Revised	Orlic-Milacic, M.
2016-02-04	Reviewed	Zaccara, S.