PI5P Regulates TP53 Acetylation

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

17/11/2022
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


Reactome database release: 82

This document contains 1 pathway and 8 reactions (see Table of Contents)

https://reactome.org
PI5P Regulates TP53 Acetylation

Stable identifier: R-HSA-6811555

Under conditions of cellular stress, nuclear levels of phosphatidylinositol-5-phosphate (PI5P) increase and, through interaction with ING2, result in nuclear retention/accumulation of ING2. ING2 binds TP53 (p53) and recruits histone acetyltransferase EP300 (p300) to TP53, leading to TP53 acetylation. Increased nuclear PI5P levels positively regulate TP53 acetylation (Ciruela et al. 2000, Gozani et al. 2003, Jones et al. 2006, Zou et al. 2007, Bultsma et al. 2010).

Literature references


Editions

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Under conditions of cellular stress, TMEM55B (type I phosphatidylinositol 4,5-bisphosphate 4-phosphatase) translocates to the nucleus through an unknown mechanism (Zou et al. 2007).

Followed by: PI(4,5)P2 is dephosphorylated to PI5P by TMEM55B in the nucleus

Literature references

PI(4,5)P2 is dephosphorylated to PI5P by TMEM55B in the nucleus

**Location:** PI5P Regulates TP53 Acetylation

**Stable identifier:** R-HSA-6810410

**Type:** transition

**Compartments:** nucleoplasm

Translocation of TMEM55B (type I phosphatidylinositol 4,5-bisphosphate 4-phosphatase) to the nucleus under conditions of cellular stress leads to dephosphorylation of nuclear PI(4,5)P2 to PI5P, thus increasing the concentration of PI5P in the nucleus (Zou et al. 2007). PIP2 and its derivatives are not associated with nuclear envelope structures (Bornenkov et al. 1998) but localize to poorly defined subnuclear compartments called nuclear specks (reviewed by Barlow et al. 2010).

**Preceded by:** TMEM55B translocates to the nucleus

**Followed by:** ING2 binds PI5P

**Literature references**


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In the nucleus, phosphatidylinositol 5-phosphate (PI5P) is phosphorylated to phosphatidylinositol 4,5-bisphosphate (PI(4,5)P2) mainly by phosphatidylinositol-5-phosphate 4-kinase type-2 beta (PIP4K2B). In the nucleus, PIP4K2B predominantly functions as a homodimer or a heterodimer with PIP4K2A. A low level of PIP4K2A homodimers can also be found in the nucleus. Nuclear localization of PIP4K2C has not been examined but is assumed to be possible, at least through formation of heterodimers with PIP4K2B (Ciruela et al. 2000, Jones et al. 2006, Bultsma et al. 2010). Under conditions of cellular stress, nuclear PIP4K2B can be phosphorylated by p38 MAP kinases, resulting in PIP4K2B inactivation. The putative p38 target site, serine residue S326 of PIP4K2B, is conserved in PIP4K2A, but the role and mechanism of p38-mediated regulation of PIP4K2 isoforms has not been studied in detail (Jones et al. 2006).

**Literature references**


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https://reactome.org
ING2 binds PI5P

Location: PI5P Regulates TP53 Acetylation

Stable identifier: R-HSA-6810376

Type: binding

Compartments: nuclear envelope, nucleoplasm

The PHD finger of ING2 binds phosphatidylinositol-5-phosphate (PI5P) (Gozani et al. 2003), which promotes nuclear retention of ING2 (Jones et al. 2006, Zou et al. 2007).

Preceded by: PI(4,5)P2 is dephosphorylated to PI5P by TMEM55B in the nucleus

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ING2 recruits histone acetyltransferase EP300 (p300) to TP53 (Padeux et al. 2005).

Followed by: ING2-bound EP300 acetylates TP53

Literature references

The histone acetyltransferase EP300 (p300), recruited to TP53 (p53) by ING2, acetylates TP53 on lysine residue K382, which may contribute to TP53-dependent apoptosis (Padeux et al. 2005). PI5P positively regulates TP53 acetylation (Zou et al. 2007), possibly by increasing the amount of ING2 in the nucleus (Gozani et al. 2003).

**Preceded by:** ING2 recruits EP300 to TP53

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https://reactome.org
MAP2K6 phosphorylates PIP4K2B

Location: PI5P Regulates TP53 Acetylation

Stable identifier: R-HSA-8877691

Type: transition

Compartments: nucleoplasm

Under conditions of cellular stress, such as increased level of reactive oxygen species, MAP2K6 (MKK6), and possibly other kinases of the p38 MAPK family, phosphorylates PIP4K2B at serine residue S326. Threonine residue T322 of PIP4K2B is also phosphorylated under stress conditions, but the responsible kinase is not known. MAP2K6 may also phosphorylate PIP4K2A, but not PIP4K2C (Kuene et al. 2012).

Followed by: PIN1 binds phosphorylated PIP4K2B

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PIN1 binds phosphorylated PIP4K2B

**Location:** PI5P Regulates TP53 Acetylation

**Stable identifier:** R-HSA-8877692

**Type:** binding

**Compartments:** nucleoplasm

Peptidyl-prolyl cis-trans isomerase PIN1 binds to PIP4K2B phosphorylated at serine residue S326. PIP4K2B is phosphorylated at S326 under conditions of cellular stress, such as increased level of reactive oxygen species (ROS). Phosphorylation of PIP4K2B at threonine residue T322 may also contribute to PIN1 binding. PIN1 induces conformational change of PIP4K2B, resulting in inactivation of PIP4K2B dimers. This enables increase of the nuclear PI5P levels. PI5P positively regulates expression of genes involved in neutralization of ROS (Keune et al. 2012).

**Preceded by:** MAP2K6 phosphorylates PIP4K2B

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</tbody>
</table>
# Table of Contents

- **Introduction**  
  - 1

- **PI5P Regulates TP53 Acetylation**  
  - TMEM55B translocates to the nucleus  
  - 2
  - PI(4,5)P2 is dephosphorylated to PI5P by TMEM55B in the nucleus  
  - 3
  - PI5P is phosphorylated to PI(4,5)P2 by PIP4K2 dimers in the nucleus  
  - 4
  - ING2 binds PI5P  
  - 5
  - ING2 recruits EP300 to TP53  
  - 6
  - ING2-bound EP300 acetylates TP53  
  - 7
  - MAP2K6 phosphorylates PIP4K2B  
  - 8
  - PIN1 binds phosphorylated PIP4K2B  
  - 9

Table of Contents  

- 11