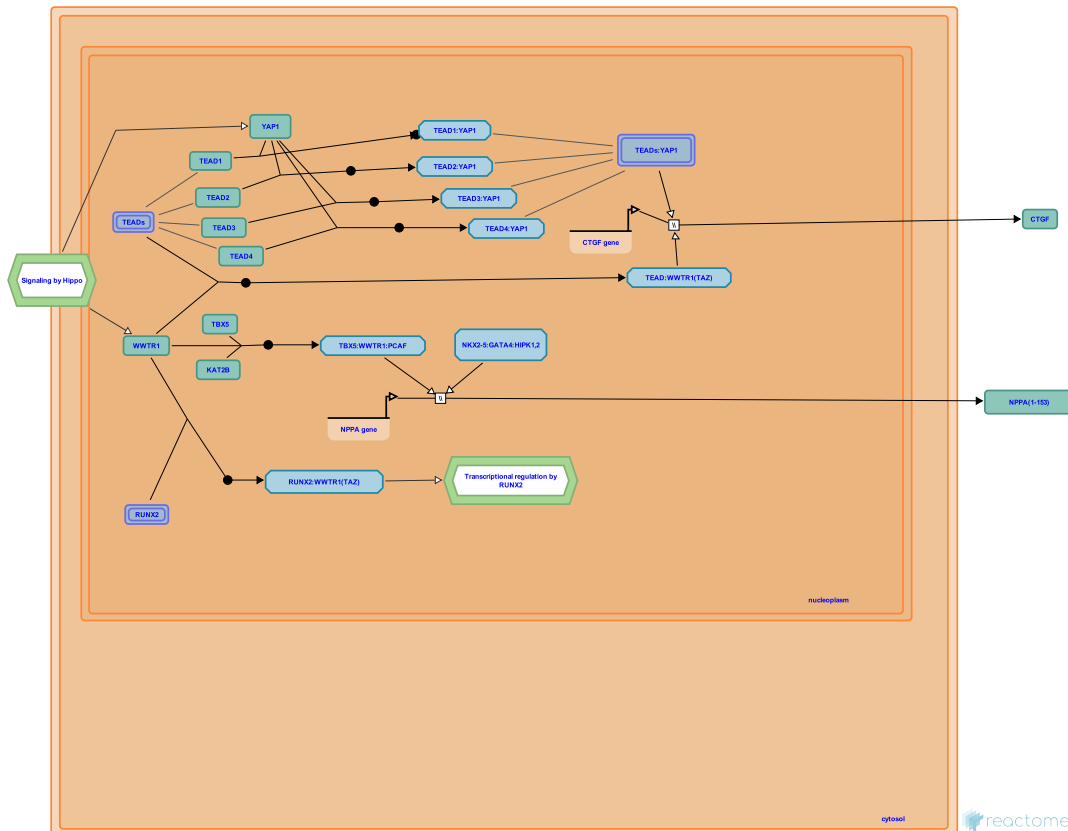


# YAP1- and WWTR1 (TAZ)-stimulated gene expression



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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.

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

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

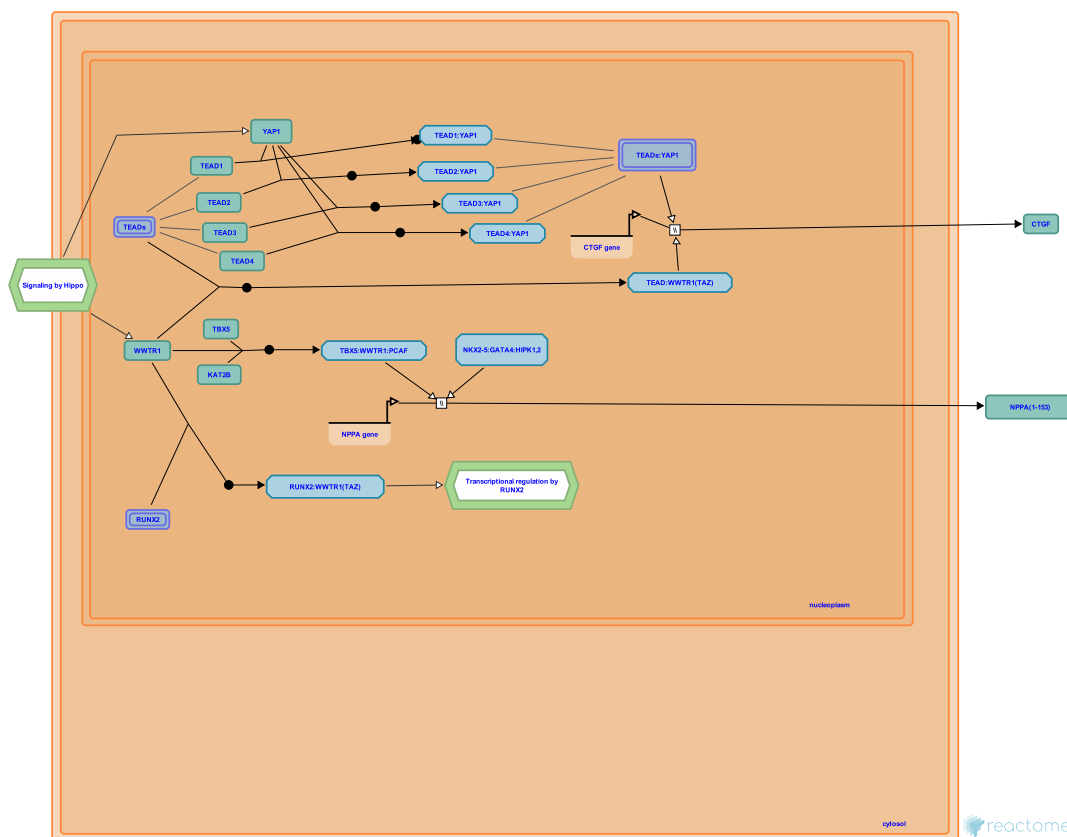
Reactome database release: 74

This document contains 1 pathway and 9 reactions ([see Table of Contents](#))

## YAP1- and WWTR1 (TAZ)-stimulated gene expression ↗

**Stable identifier:** R-HSA-2032785

**Compartments:** cytosol, nucleoplasm



YAP1 and WWTR1 (TAZ) are transcriptional co-activators, both homologues of the *Drosophila* Yorkie protein. They both interact with members of the TEAD family of transcription factors, and WWTR1 interacts as well with TBX5 and RUNX2, to promote gene expression. Their transcriptional targets include genes critical to regulation of cell proliferation and apoptosis. Their subcellular location is regulated by the Hippo signaling cascade: phosphorylation mediated by this cascade leads to the cytosolic sequestration of both proteins (Murakami et al. 2005; Oh and Irvine 2010).

### Literature references

Murakami, M., Nakagawa, M., Olson, EN., Nakagawa, O. (2005). A WW domain protein TAZ is a critical coactivator for TBX5, a transcription factor implicated in Holt-Oram syndrome. *Proc Natl Acad Sci U S A*, 102, 18034-9. ↗

Oh, H., Irvine, KD. (2010). Yorkie: the final destination of Hippo signaling. *Trends Cell Biol*, 20, 410-7. ↗

### Editions

2012-01-07	Edited	D'Eustachio, P.
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2012-02-03	Reviewed	Sudol, M.

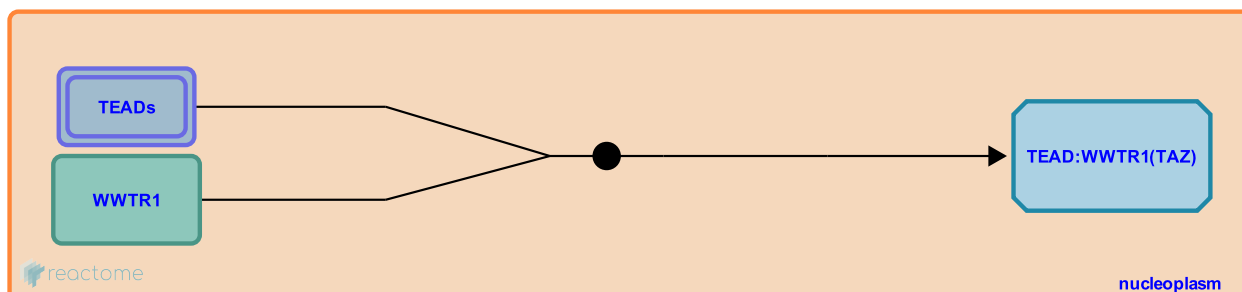
## WWTR1 (TAZ) binds TEAD [↗](#)

**Location:** [YAP1- and WWTR1 \(TAZ\)-stimulated gene expression](#)

**Stable identifier:** R-HSA-2032781

**Type:** binding

**Compartments:** nucleoplasm



In the nucleus the WWTR1 (TAZ) transcriptional coactivator can bind any one of the four TEAD transcription factors to form a complex. The stoichiometry of this complex is unknown (Chan et al. 2009; Zhang et al. 2009).

**Followed by:** [Expression of CTGF](#)

### Literature references

Chan, SW., Lim, CJ., Loo, LS., Chong, YF., Huang, C., Hong, W. (2009). TEADs mediate nuclear retention of TAZ to promote oncogenic transformation. *J Biol Chem*, 284, 14347-58. [↗](#)

Zhang, H., Liu, CY., Zha, ZY., Zhao, B., Yao, J., Zhao, S. et al. (2009). TEAD transcription factors mediate the function of TAZ in cell growth and epithelial-mesenchymal transition. *J Biol Chem*, 284, 13355-62. [↗](#)

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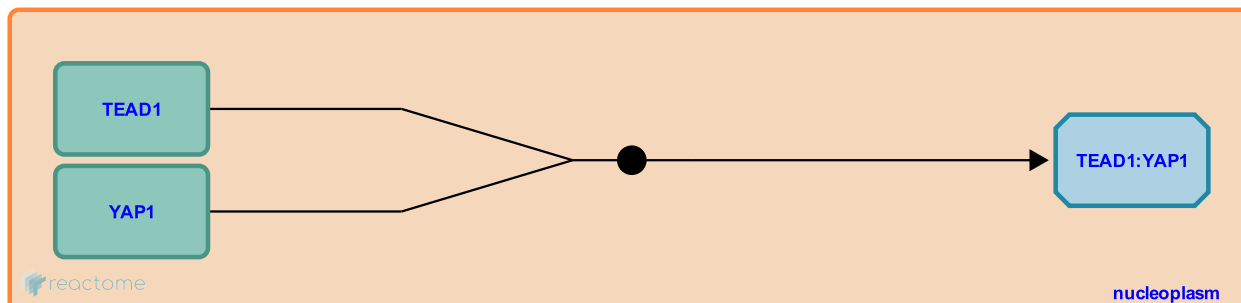
## YAP1 binds TEAD1 ↗

**Location:** [YAP1- and WWTR1 \(TAZ\)-stimulated gene expression](#)

**Stable identifier:** R-HSA-2032775

**Type:** binding

**Compartments:** nucleoplasm



In the nucleus the YAP1 transcriptional coactivator can bind any one of the four TEAD transcription factors to form a complex. The stoichiometry of this complex is unknown (Chan et al. 2009).

**Followed by:** [Expression of CTGF](#)

## Literature references

Chan, SW., Lim, CJ., Loo, LS., Chong, YF., Huang, C., Hong, W. (2009). TEADs mediate nuclear retention of TAZ to promote oncogenic transformation. *J Biol Chem*, 284, 14347-58. ↗

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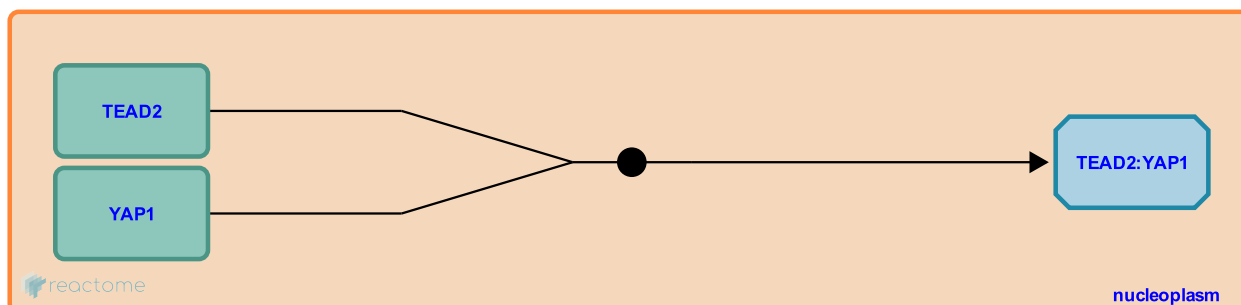
## YAP1 binds TEAD2 ↗

**Location:** [YAP1- and WWTR1 \(TAZ\)-stimulated gene expression](#)

**Stable identifier:** R-HSA-8871260

**Type:** binding

**Compartments:** nucleoplasm



The YAP1 transcriptional coactivator can bind any one of the four TEAD transcription factors to form a complex. The stoichiometry of this complex is unknown (Chan et al. 2009).

### Literature references

Chan, SW., Lim, CJ., Loo, LS., Chong, YF., Huang, C., Hong, W. (2009). TEADs mediate nuclear retention of TAZ to promote oncogenic transformation. *J Biol Chem*, 284, 14347-58. ↗

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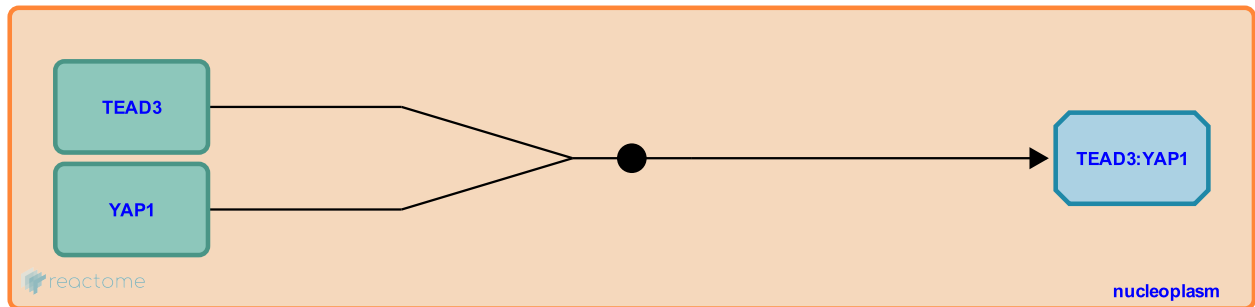
## YAP1 binds TEAD3 [↗](#)

**Location:** [YAP1- and WWTR1 \(TAZ\)-stimulated gene expression](#)

**Stable identifier:** R-HSA-8871266

**Type:** binding

**Compartments:** nucleoplasm



YAP1 is a transcriptional coactivator that can bind any one of the four TEAD transcription factors to form a complex. The stoichiometry of this complex is unknown (Chan et al. 2009).

### Literature references

Chan, SW., Lim, CJ., Loo, LS., Chong, YF., Huang, C., Hong, W. (2009). TEADs mediate nuclear retention of TAZ to promote oncogenic transformation. *J Biol Chem*, 284, 14347-58. [↗](#)

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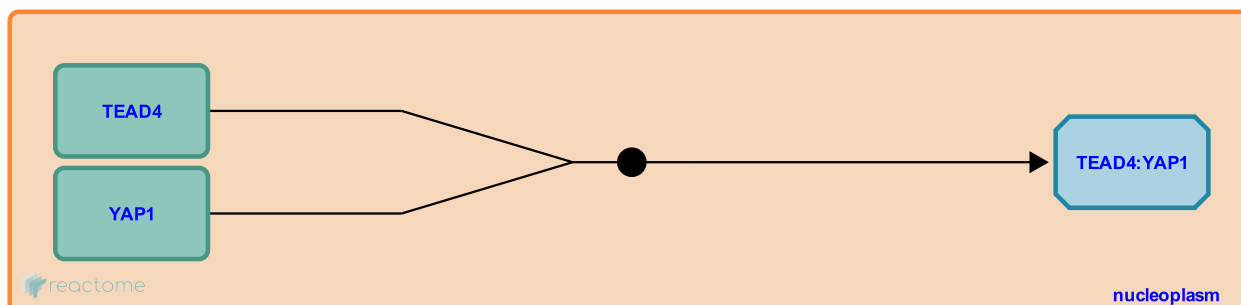
## YAP1 binds TEAD4 ↗

**Location:** YAP1- and WWTR1 (TAZ)-stimulated gene expression

**Stable identifier:** R-HSA-8871265

**Type:** binding

**Compartments:** nucleoplasm



The YAP1 transcriptional coactivator can bind any one of the four TEAD family transcription factors to form a complex. The stoichiometry of this complex is unknown (Chan et al. 2009).

### Literature references

Chan, SW., Lim, CJ., Loo, LS., Chong, YF., Huang, C., Hong, W. (2009). TEADs mediate nuclear retention of TAZ to promote oncogenic transformation. *J Biol Chem*, 284, 14347-58. ↗

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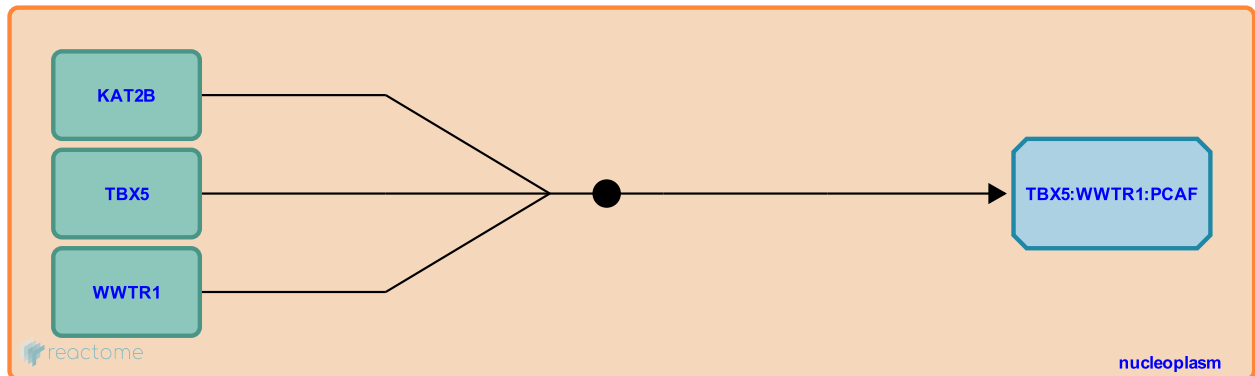
## WWTR1 (TAZ), TBX5, and PCAF form a complex ↗

**Location:** [YAP1- and WWTR1 \(TAZ\)-stimulated gene expression](#)

**Stable identifier:** R-HSA-2032794

**Type:** binding

**Compartments:** nucleoplasm



In the nucleus the WWTR1 (TAZ) transcriptional coactivator can bind the TBX5 transcription factor and PCAF (KAT2B) histone acetyltransferase to form a complex. The stoichiometry of this complex is unknown (Murakami et al. 2005).

**Followed by:** [Expression of NPPA \(ANF\)](#)

### Literature references

Murakami, M., Nakagawa, M., Olson, EN., Nakagawa, O. (2005). A WW domain protein TAZ is a critical coactivator for TBX5, a transcription factor implicated in Holt-Oram syndrome. *Proc Natl Acad Sci U S A*, 102, 18034-9. ↗

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## WWTR1 (TAZ) binds RUNX2 [↗](#)

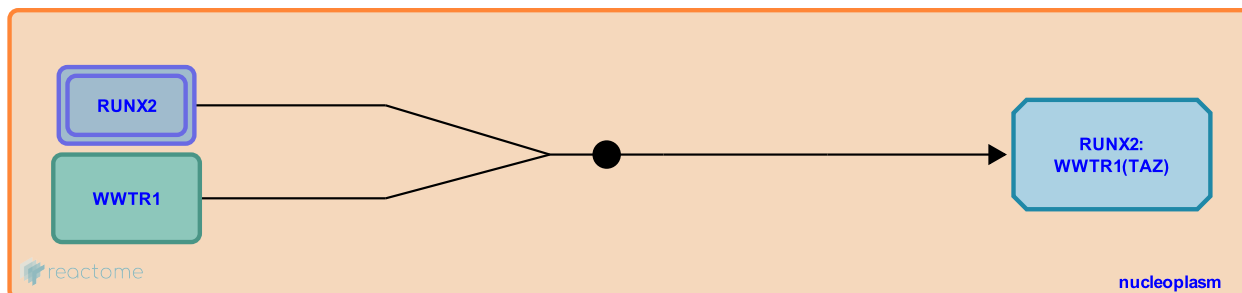
**Location:** [YAP1- and WWTR1 \(TAZ\)-stimulated gene expression](#)

**Stable identifier:** R-HSA-2064932

**Type:** binding

**Compartments:** nucleoplasm

**Inferred from:** [Wwtr1 \(Taz\) binds Runx2 \(Mus musculus\)](#)



In the nucleus the WWTR1 (TAZ) transcriptional coactivator can bind the RUNX2 transcription factor to form a complex. This interaction has not been experimentally characterized in human cells but is inferred from properties of the homologous mouse proteins. The stoichiometry of this complex is unknown (Cui et al. 2003).

Formation of the RUNX2:WWTR1 complex is implicated in promotion of luminal breast cancer progression through regulation of E-cadherin (CDH1) and cross-talk with ERBB2 (HER2) signaling (Brusgard et al. 2015).

### Literature references

Cui, CB., Cooper, LF., Yang, X., Karsenty, G., Aukhil, I. (2003). Transcriptional coactivation of bone-specific transcription factor Cbfa1 by TAZ. *Mol Cell Biol*, 23, 1004-13. [↗](#)

Hong, JH., Hwang, ES., McManus, MT., Amsterdam, A., Tian, Y., Kalmukova, R. et al. (2005). TAZ, a transcriptional modulator of mesenchymal stem cell differentiation. *Science*, 309, 1074-8. [↗](#)

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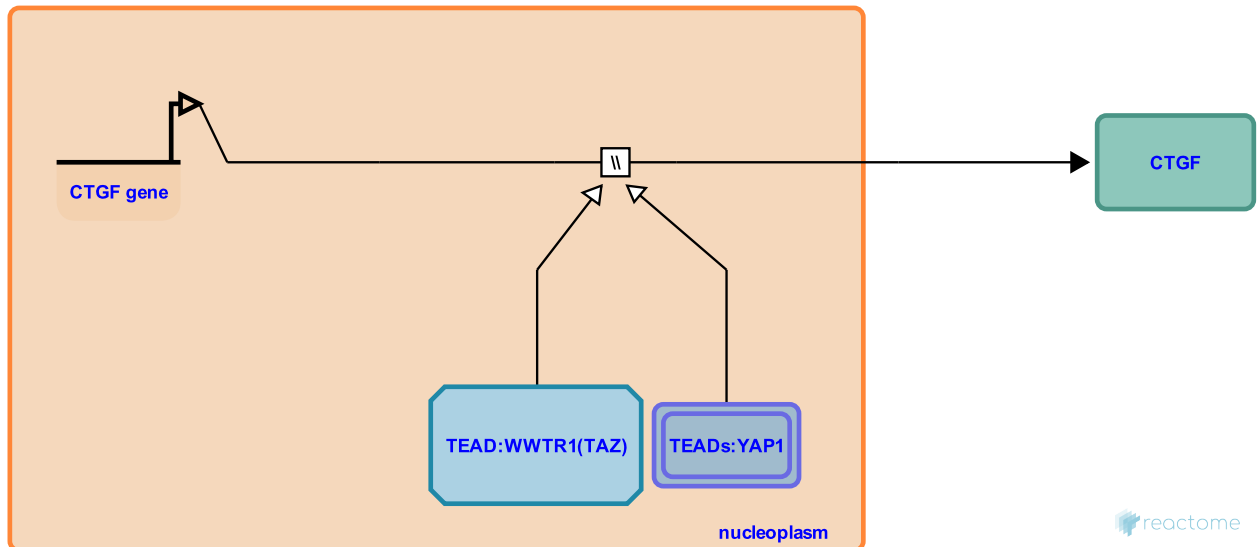
## Expression of CTGF ↗

**Location:** [YAP1- and WWTR1 \(TAZ\)-stimulated gene expression](#)

**Stable identifier:** R-HSA-1989766

**Type:** omitted

**Compartments:** nucleoplasm, extracellular region



The CTGF gene is transcribed to yield mRNA and the mRNA is translated to yield protein. Transcription of the CTGF gene is increased by both YAP1:TEAD and WWTR1(TAZ):TEAD transcriptional coactivator:transcription factor complexes, so that CTGF is one of the many genes whose expression is downregulated by the action of the hippo cascade (Zhang et al. 2009; Zhao et al. 2008).

**Preceded by:** [WWTR1 \(TAZ\) binds TEAD](#), [YAP1 binds TEAD1](#)

## Literature references

- van der Meer, DL., Degenhardt, T., Vaisanen, S., de Groot, PJ., Heinaniemi, M., de Vries, SC. et al. (2010). Profiling of promoter occupancy by PPAR{alpha} in human hepatoma cells via ChIP-chip analysis. *Nucleic Acids Res.* ↗
- Zhang, H., Liu, CY., Zha, ZY., Zhao, B., Yao, J., Zhao, S. et al. (2009). TEAD transcription factors mediate the function of TAZ in cell growth and epithelial-mesenchymal transition. *J Biol Chem*, 284, 13355-62. ↗
- Chan, SW., Lim, CJ., Loo, LS., Chong, YF., Huang, C., Hong, W. (2009). TEADs mediate nuclear retention of TAZ to promote oncogenic transformation. *J Biol Chem*, 284, 14347-58. ↗
- Zhao, B., Ye, X., Yu, J., Li, L., Li, W., Li, S. et al. (2008). TEAD mediates YAP-dependent gene induction and growth control. *Genes Dev.*, 22, 1962-71. ↗

## Editions

2009-06-08	Reviewed	Kersten, S.
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2017-01-31	Reviewed	Ito, Y., Chuang, LS.
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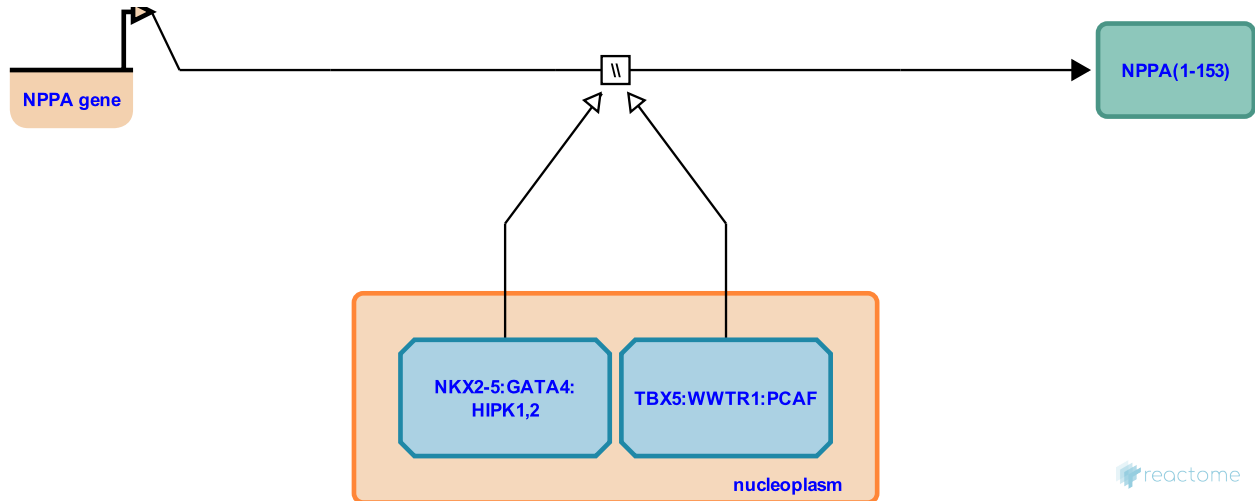
## Expression of NPPA (ANF) ↗

**Location:** [YAP1- and WWTR1 \(TAZ\)-stimulated gene expression](#)

**Stable identifier:** R-HSA-2032800

**Type:** omitted

**Compartments:** extracellular region



Transcription of the NPPA (ANF) gene is stimulated by the action of a transcription factor complex that includes WWTR1 (TAZ), TBX5, and the PCAF (KAT2B) histone acetyltransferase (Murakami et al. 2005). Homeobox protein NKX-2.5 (NKX2-5), in cooperation with transcription factor GATA-4 (GATA4) and interacting partners homeodomain-interacting protein kinase 1 and 2 (HIPK1 and 2), acts as a transcriptional activator factor of NPPA in mice (Lee et al. 1998). Defects in NKX2-5 can cause diverse cardiac developmental disorders (Schott et al. 1998, Benson et al. 1999).

**Preceded by:** [WWTR1 \(TAZ\), TBX5, and PCAF form a complex](#)

## Literature references

- Murakami, M., Nakagawa, M., Olson, EN., Nakagawa, O. (2005). A WW domain protein TAZ is a critical coactivator for TBX5, a transcription factor implicated in Holt-Oram syndrome. *Proc Natl Acad Sci U S A*, 102, 18034-9. ↗
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- Benson, DW., Silberbach, GM., Kavanaugh-McHugh, A., Cottrill, C., Zhang, Y., Riggs, S. et al. (1999). Mutations in the cardiac transcription factor NKX2.5 affect diverse cardiac developmental pathways. *J. Clin. Invest.*, 104, 1567-73. ↗

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# Table of Contents

Introduction	1
☰ YAP1- and WWTR1 (TAZ)-stimulated gene expression	2
↳ WWTR1 (TAZ) binds TEAD	3
↳ YAP1 binds TEAD1	4
↳ YAP1 binds TEAD2	5
↳ YAP1 binds TEAD3	6
↳ YAP1 binds TEAD4	7
↳ WWTR1 (TAZ), TBX5, and PCAF form a complex	8
↳ WWTR1 (TAZ) binds RUNX2	9
☰ Expression of CTGF	10
☰ Expression of NPPA (ANF)	11
Table of Contents	12