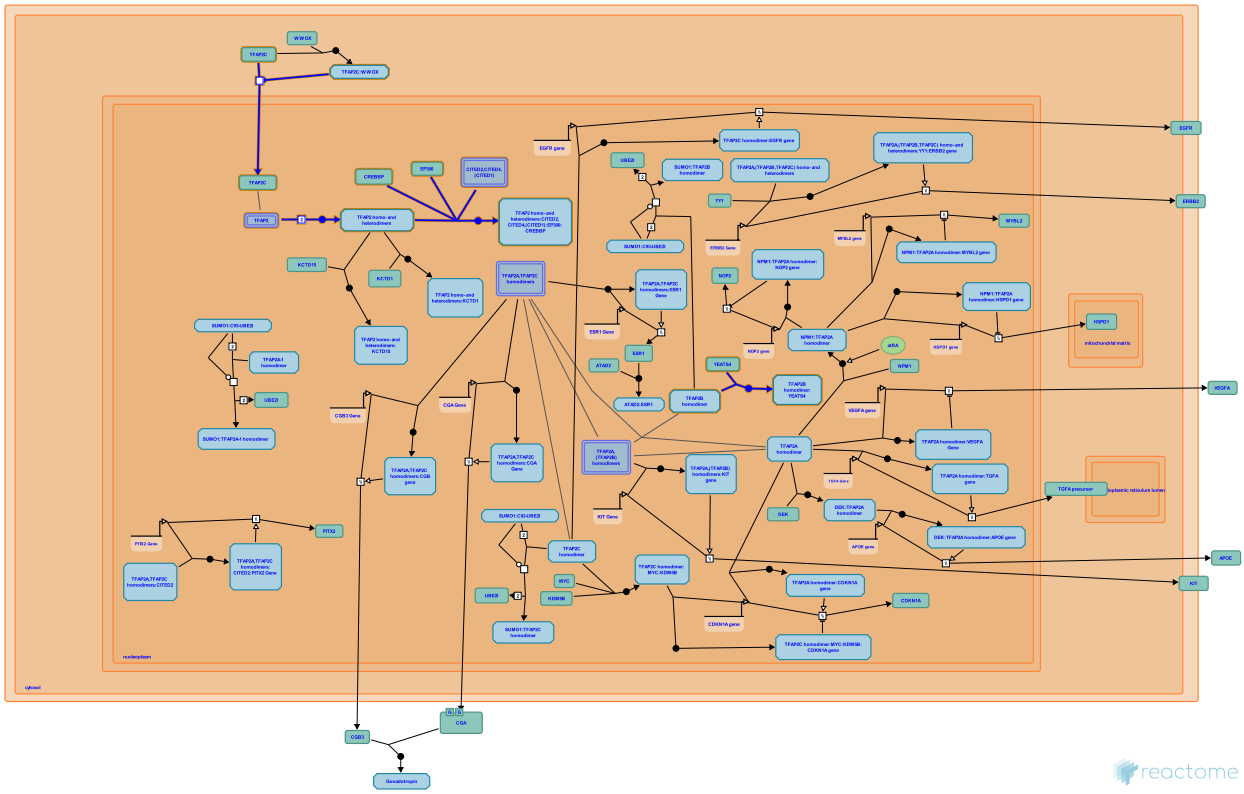
Activation of the TFAP2 (AP-2) family of transcription factors



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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. ↗

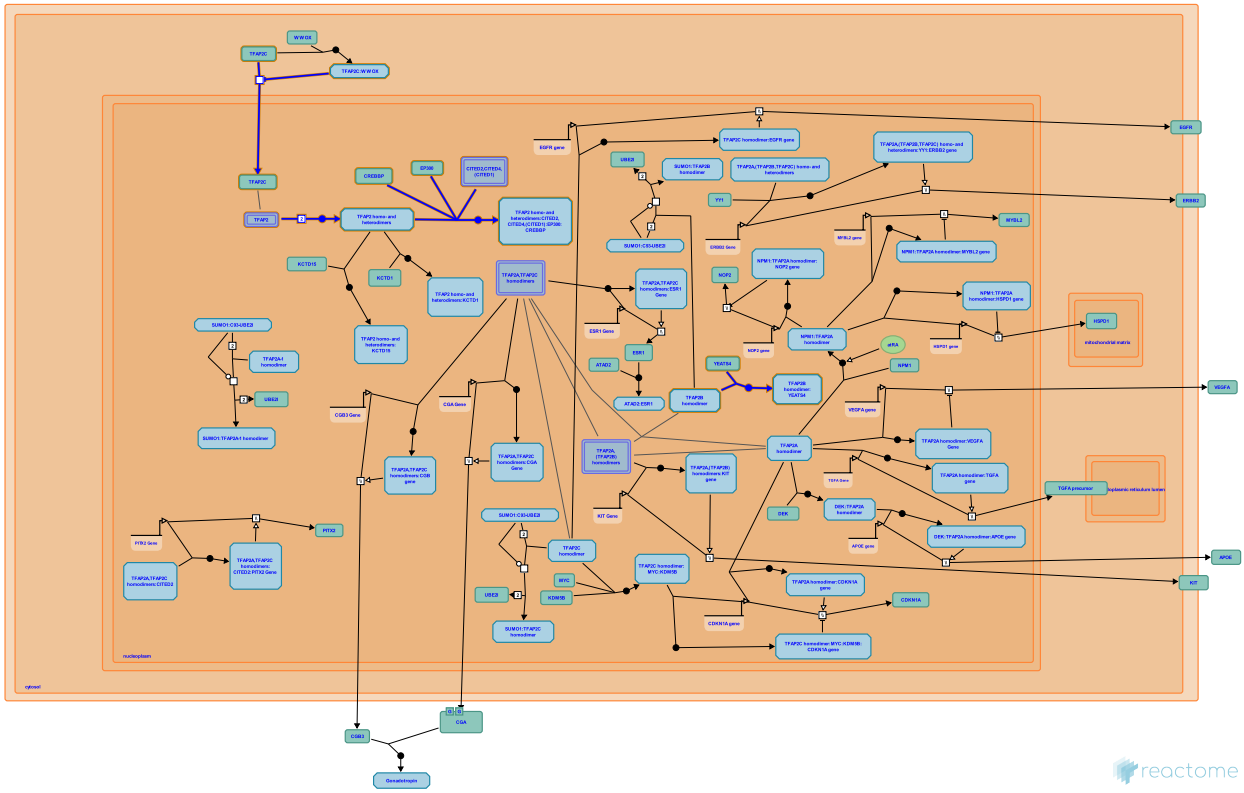
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Activation of the TFAP2 (AP-2) family of transcription factors ↗

Stable identifier: R-HSA-8866907



The helix-span-helix motif and the basic region of TFAP2 (AP-2) transcription factor family members TFAP2A, TFAP2B, TFAP2C, TFAP2D and TFAP2E enable dimerization and DNA binding. AP-2 dimers bind palindromic GC-rich DNA response elements that match the consensus sequence 5'-GCCNNNGGC-3' (Williams and Tjian 1991a, Williams and Tjian 1991b). Most of the AP-2 binding sites slightly differ from the consensus, and individual AP-2 family members may differ in their binding site preferences (McPherson and Weigel 1999, Orso et al. 2010). Transcriptional co-factors from the CITED family interact with the helix-span-helix (HSH) domain of TFAP2 (AP-2) family of transcription factors and recruit transcription co-activators EP300 (p300) and CREBBP (CBP) to TFAP2-bound DNA elements. CITED2 shows the highest affinity for TFAP2 proteins, followed by CITED4, while CITED1 interacts with TFAP2s with a very low affinity. Mouse embryos defective for CITED2 exhibit neural crest defects, cardiac malformations and adrenal agenesis, which can at least in part be attributed to a defective Tfap2 transactivation (Bamforth et al. 2001, Braganca et al. 2002, Braganca et al. 2003). DNA binding and transcriptional activity of TFAP2B homodimers is increased by binding to YEATS4 (GAS41) (Ding et al. 2006).

Literature references

Eloranta, JJ., Swingler, T., Bhattacharya, S., Shioda, T., Hurst, HC., Bragança, J. et al. (2002). Human CREB-binding protein/p300-interacting transactivator with ED-rich tail (CITED) 4, a new member of the CITED family, functions as a co-activator for transcription factor AP-2. *J. Biol. Chem., 277*, 8559-65. ↗

Tjian, R., Williams, T. (1991). Characterization of a dimerization motif in AP-2 and its function in heterologous DNA-binding proteins. *Science, 251*, 1067-71. ↗

Tjian, R., Williams, T. (1991). Analysis of the DNA-binding and activation properties of the human transcription factor AP-2. *Genes Dev., 5*, 670-82. ↗

Weigel, RJ., McPherson, LA. (1999). AP2alpha and AP2gamma: a comparison of binding site specificity and trans-activation of the estrogen receptor promoter and single site promoter constructs. *Nucleic Acids Res., 27*, 4040-9. ↗

Bamforth, SD., Bragança, J., Bhattacharya, S., Murdoch, JN., Marques, FI., Farza, H. et al. (2001). Cardiac malformations, adrenal agenesis, neural crest defects and exencephaly in mice lacking Cited2, a new Tfap2 co-activator. *Nat. Genet., 29*, 469-74. ↗

Editions

2016-03-14	Authored, Edited	Orlic-Milacic, M.
2016-05-04	Reviewed	Dawid, IB., Zarelli, VE.
2016-05-17	Reviewed	Weigel, RJ., Bogachek, MV.

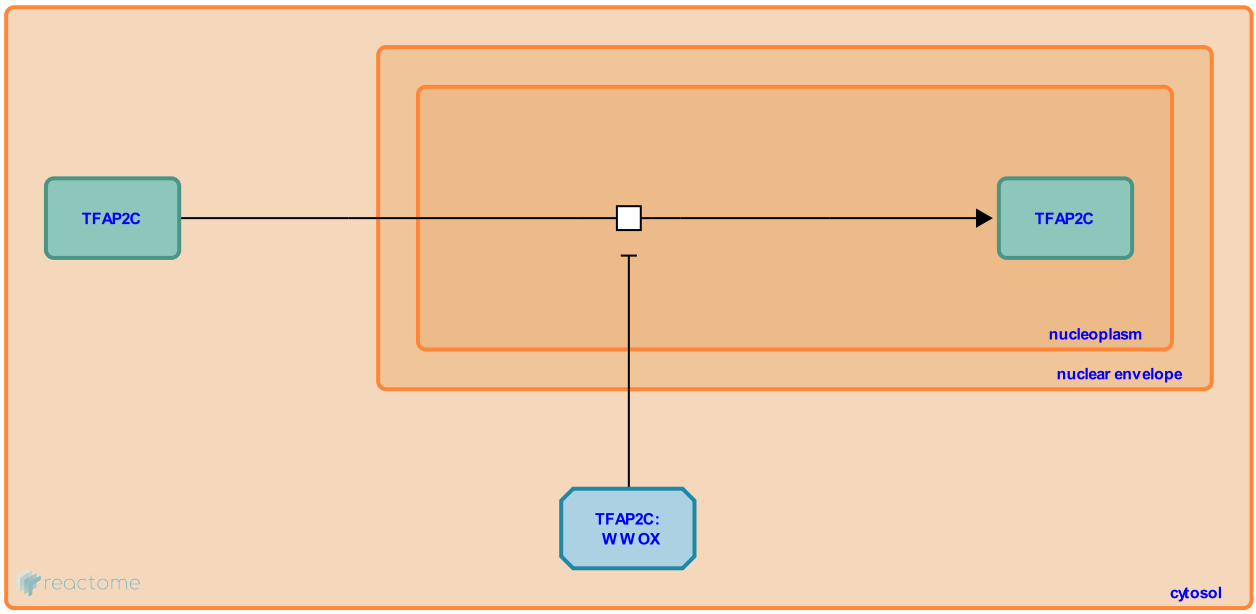
TFAP2C translocates to the nucleus ↗

Location: Activation of the TFAP2 (AP-2) family of transcription factors

Stable identifier: R-HSA-8864577

Type: transition

Compartments: nucleoplasm, cytosol



Like other AP-2 (TFAP2) transcription factor family members, TFAP2C (AP-2 gamma) mainly localizes to the nucleus. WWOX inhibits nuclear translocation of TFAP2C (Aqeilan et al. 2004).

Followed by: AP-2 (TFAP2) transcription factors form homo- and heterodimers

Literature references

Weigel, RJ., Palamarchuk, A., Herrero, JJ., Aqeilan, RI., Croce, CM., Pekarsky, Y. (2004). Physical and functional interactions between the Wwox tumor suppressor protein and the AP-2gamma transcription factor. *Cancer Res., 64*, 8256-61. ↗

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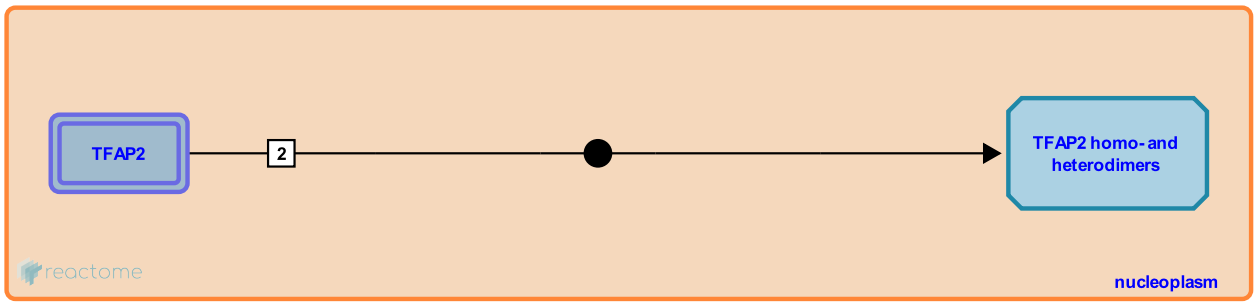
AP-2 (TFAP2) transcription factors form homo- and heterodimers ↗

Location: Activation of the TFAP2 (AP-2) family of transcription factors

Stable identifier: R-HSA-8864278

Type: binding

Compartments: nucleoplasm



AP-2 family transcription factors (TFAP2) bind palindromic DNA response elements as dimers. AP-2 family members are able to form homo- and heterodimers through the interaction of their C-terminal helix-span-helix (HSH) motifs. Both HSH motifs and centrally located basic regions are needed for DNA binding (Williams and Tjian 1991a, Williams and Tjian 1991b).

Preceded by: TFAP2C translocates to the nucleus

Followed by: TFAP2B homodimer binds YEATS4, TFAP2 homo- and heterodimers bind CITED and EP300/CREBBP

Literature references

Tjian, R., Williams, T. (1991). Characterization of a dimerization motif in AP-2 and its function in heterologous DNA-binding proteins. *Science, 251*, 1067-71. ↗

Tjian, R., Williams, T. (1991). Analysis of the DNA-binding and activation properties of the human transcription factor AP-2. *Genes Dev., 5*, 670-82. ↗

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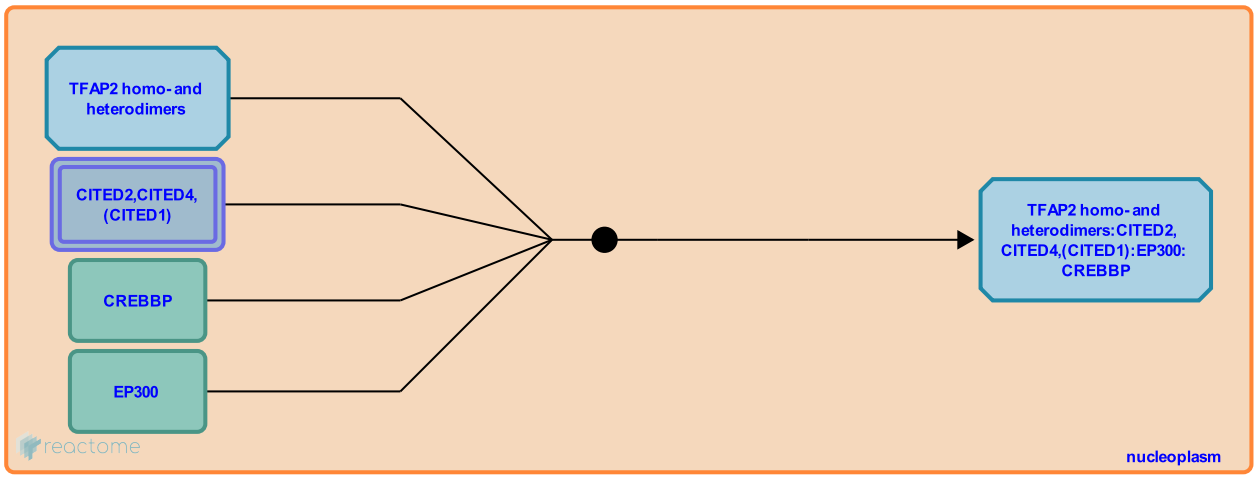
TFAP2 homo- and heterodimers bind CITED and EP300/CREBBP ↗

Location: Activation of the TFAP2 (AP-2) family of transcription factors

Stable identifier: R-HSA-8864307

Type: binding

Compartments: nucleoplasm



Transcriptional co-factors from the CITED family interact with the helix-span-helix (HSH) domain of TFAP2 (AP-2) family of transcription factors and recruit transcription co-activators EP300 (p300) and CREBBP (CBP) to TFAP2-bound DNA elements. CITED2 shows the highest affinity for TFAP2 proteins, followed by CITED4, while CITED1 interacts with TFAP2s with a very low affinity. The interaction with CITED proteins was specifically demonstrated for TFAP2A (AP-2 alpha), TFAP2B (AP2-beta) and TFAP2C (AP-2 gamma), and is extrapolated to TFAP2D (AP2-delta) and TFAP2E (AP-2 epsilon) based on sequence similarity (Braganca et al. 2002, Braganca et al. 2003). Mouse embryos defective for CITED2 exhibit neural crest defects, cardiac malformations and adrenal agenesis, which can at least in part be attributed to defective Tfap2 transactivation (Bamforth et al. 2001).

Preceded by: AP-2 (TFAP2) transcription factors form homo- and heterodimers

Literature references

Eloranta, JJ., Swingler, T., Bhattacharya, S., Shioda, T., Hurst, HC., Bragança, J. et al. (2002). Human CREB-binding protein/p300-interacting transactivator with ED-rich tail (CITED) 4, a new member of the CITED family, functions as a co-activator for transcription factor AP-2. *J. Biol. Chem., 277*, 8559-65. ↗

Bamforth, SD., Bragança, J., Bhattacharya, S., Murdoch, JN., Marques, FI., Farza, H. et al. (2001). Cardiac malformations, adrenal agenesis, neural crest defects and exencephaly in mice lacking Cited2, a new Tfap2 co-activator. *Nat. Genet., 29*, 469-74. ↗

Eloranta, JJ., Bhattacharya, S., Hurst, HC., Ibbitt, JC., Bragança, J., Bamforth, SD. (2003). Physical and functional interactions among AP-2 transcription factors, p300/CREB-binding protein, and CITED2. *J. Biol. Chem., 278*, 16021-9 . ↗

Editions

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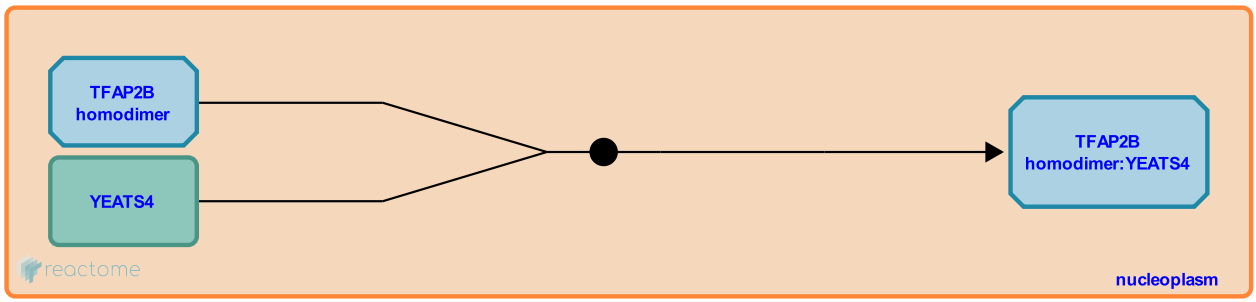
TFAP2B homodimer binds YEATS4 ↗

Location: Activation of the TFAP2 (AP-2) family of transcription factors

Stable identifier: R-HSA-8864595

Type: binding

Compartments: nucleoplasm



TFAP2B (AP-2 beta) binds YEATS4 (GAS41). Formation of the TFAP2B:YEATS4 complex increases DNA binding and transcriptional activity of TFAP2B homodimers (Ding et al. 2006).

Preceded by: AP-2 (TFAP2) transcription factors form homo- and heterodimers

Literature references

Zhang, J., Feng, D., Fan, C., Ding, X., Zhou, J., Ren, K. et al. (2006). GAS41 interacts with transcription factor AP-2beta and stimulates AP-2beta-mediated transactivation. *Nucleic Acids Res., 34*, 2570-8. ↗

Editions

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