Expression of PPARG

D'Eustachio, P., Gopinathrao, G., May, B., Sethi, JK.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

03/05/2024

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. ↗

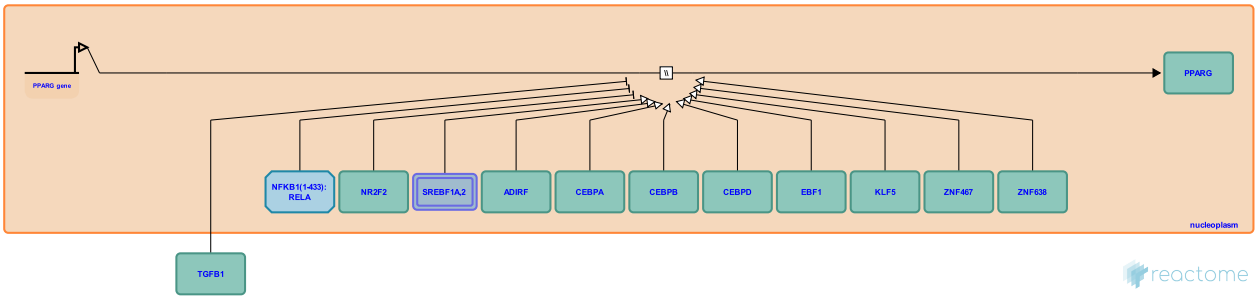
Expression of PPARG ↗

Stable identifier: R-HSA-381283

Type: omitted

Compartments: nucleoplasm

Inferred from: Expression of Pparg (Mus musculus)



As inferred from mouse homologs, ZNF467 (ZFP467) binds the promoter of the PPARG gene and recruits a histone deacetylase complex to activate transcription of PPARG.
Activation of PPARG transcription by CEPBA is inferred from mouse.
As inferred from mouse, NF-kappaB inhibits expression of PPARG in pre-adipocytes (Chae and Kwak 2003). TNFalpha represses PPARG via NF-kappaB (Chae and Kwak 2003, Kurebayashi et al. 2001, Xing et al. 1997).
The transcription factors CEBPB, CEBPD, and KLF5 simultaneously bind the PPARG promoter and synergistically activate transcription of the PPARG gene. These three factors activate transcription after initial stimulation of adipocyte differentiation but then are replaced by CEBPA within 10 days. CEBPA and other factors may be responsible for long term maintenance of PPARG expression and the differentiated state.
Pre-adipose tissue contains both the widely expressed PPARG isoform 1 mRNA and the more tissue-specific PPARG isoform 2. The PPARG isoform 2 mRNA is translated to yield PPARG isoform 2 protein, which has 505 amino acid residues (57 KDa) and is the longest of the 4 observed variants. Isoform 2 is specific to preadipose and adipose tissue (Mukherjee et al. 1997). Confusingly, the longest variant is called isoform 1 in some publications.
In mouse, by 10 days after induction of adipocyte differentiation Cebpa, but neither Cebpb nor Cebpd, is detectable at the Pparg promoter. While adipocyte differentiation can proceed without Cebpa, adipocytes differentiated from Cebpa-knockout cells are insulin insensitive due to a defect in Glut4 (Slc2a4) vesicle trafficking.
The adipogenesis regulatory factor (ADIRF, aka AFRO, APM2, C10orf116) promotes adipogenic differentiation and stimulates transcription initiation of master adipogenesis factors like PPARG and CEBPA (Ni et al. 2013).
As inferred from mouse, SREBP1A and SREBP2 bind to the PPARG1 and PPARG2 promoters and activate transcription.
As inferred from mouse, TGF-beta inhibits expression of PPARG.
ZNF638 cooperates together with CEBPB and CEBPD at the promoter of the PPARG gene to activate transcription (inferred from mouse homologs).
As inferred from mouse 3T3-L1 cells, Wnt-1 and Wnt-10b inhibit PPARG expression (Ross et al. 2000, Bennett et al. 2002) by activating COUP-TFII (NR2F2) which recruits the SMRT repressor complex to the PPARG gene (Okamura et al. 2009).

Literature references

Paterniti JR, Jr., Croston, GE., Jow, L., Mukherjee, R. (1997). Identification, characterization, and tissue distribution of human peroxisome proliferator-activated receptor (PPAR) isoforms PPARgamma2 versus PPARgamma1 and activation with retinoid X receptor agonists and antagonists. *J Biol Chem, 272*, 8071-6. ↗

Vidal-Puig, A., O'Rahilly, S., Blows, F., Sewter, CP. (2002). Regional differences in the response of human pre-adipocytes to PPARgamma and RXRalpha agonists. *Diabetes, 51*, 718-23. ↗

Guo, X., Ni, Y., Qiu, J., Wang, B., Ji, C., Wang, J. (2013). A Novel pro-adipogenesis factor abundant in adipose tissues and over-expressed in obesity acts upstream of PPARγ and C/EBPα. *J. Bioenerg. Biomembr., 45*, 219-28. ↗

Farmer, SR. (2006). Transcriptional control of adipocyte formation. *Cell Metab, 4*, 263-73. ↗

Editions

2008-11-20	Edited	Gopinathrao, G., May, B.
2009-05-15	Authored, Edited	May, B.
2009-05-27	Reviewed	D'Eustachio, P.
2011-02-10	Reviewed	Sethi, JK.