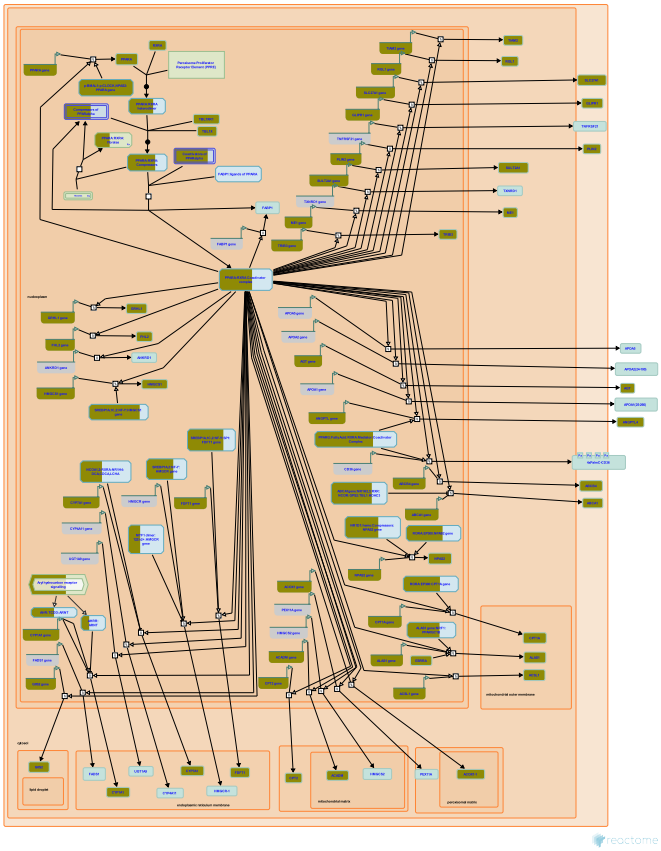
Regulation of lipid metabolism by PPARalpha



Huddart, R., Jassal, B., Kersten, S., Matthews, L., May, B., Somers, J.

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

26/09/2024

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. ↗

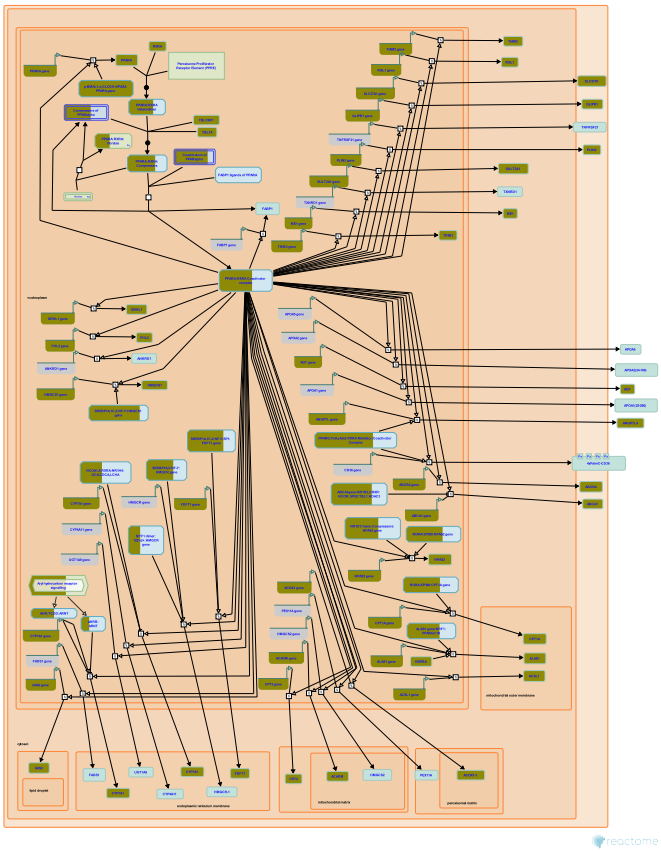
Analysis properties

- This is an **overrepresentation** analysis: A statistical (hypergeometric distribution) test that determines whether certain Reactome pathways are over-represented (enriched) in the submitted data. It answers the question 'Does my list contain more proteins for pathway X than would be expected by chance?' This test produces a probability score, which is corrected for false discovery rate using the Benjamani-Hochberg method.
  See more
- 6189 out of 10999 identifiers in the sample were found in Reactome, where 2484 pathways were hit by at least one of them.
- All non-human identifiers have been converted to their human equivalent. ↗
- This report is filtered to show only results for species 'Homo sapiens' and resource 'all resources'.
- The unique ID for this analysis (token) is MjAyNDA4MjQyMzM4NDJfMTU4MTA%3D. This ID is valid for at least 7 days in Reactome's server. Use it to access Reactome services with your data.

Regulation of lipid metabolism by PPARalpha ↗

Stable identifier: R-HSA-400206

Compartments: nucleoplasm, cytosol



Peroxisome proliferator-activated receptor alpha (PPAR-alpha) is the major regulator of fatty acid oxidation in the liver. PPARalpha is also the target of fibrate drugs used to treat abnormal plasma lipid levels.
PPAR-alpha is a type II nuclear receptor (its subcellular location does not depend on ligand binding). PPAR-alpha forms heterodimers with Retinoid X receptor alpha (RXR-alpha), another type II nuclear receptor. PPAR-alpha is activated by binding fatty acid ligands, especially polyunsaturated fatty acids having 18-22 carbon groups and 2-6 double bonds.
The PPAR-alpha:RXR-alpha heterodimer binds peroxisome proliferator receptor elements (PPREs) in and around target genes. Binding of fatty acids and synthetic ligands causes a conformational change in PPAR-alpha such that it releases the corepressors and binds coactivators (CBP-SRC-HAT complex, ASC complex, and TRAP-Mediator complex) which initiate transcription of the target genes.
Target genes of PPAR-alpha participate in fatty acid transport, fatty acid oxidation, triglyceride clearance, lipoprotein production, and cholesterol homeostasis.

Literature references

Gouni-Berthold, I., Krone, W. (2005). Peroxisome proliferator-activated receptor alpha (PPARalpha) and atherosclerosis. *Curr Drug Targets Cardiovasc Haematol Disord, 5*, 513-23. ↗

Gelman, L., Wahli, W., Michalik, L., Desvergne, B., Feige, JN. (2006). From molecular action to physiological outputs: peroxisome proliferator-activated receptors are nuclear receptors at the crossroads of key cellular functions. *Prog Lipid Res, 45*, 120-59. ↗

Wahli, W., Desvergne, B. (1999). Peroxisome proliferator-activated receptors: nuclear control of metabolism. *Endocr Rev, 20*, 649-88. ↗

Kersten, S. (2008). Peroxisome proliferator activated receptors and lipoprotein metabolism. *PPAR Res, 2008*, 132960. ↗

Editions

2009-05-30	Authored, Edited	May, B.
2009-06-08	Reviewed	Kersten, S.
2009-06-08	Edited	May, B.
2011-11-08	Edited	May, B.
2011-11-13	Revised	May, B.

82 submitted entities found in this pathway, mapping to 110 Reactome entities

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
ENSG00000001167	P23511	ENSG00000005339	Q92793	ENSG00000005471	P21439
ENSG00000008838	O75448	ENSG00000023330	P13196	ENSG00000025434	Q13133
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ENSG00000100393	Q09472	ENSG00000101255	Q96RU7	ENSG00000101849	O60907
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ENSG00000106546	P35869	ENSG00000108510	Q9UHV7	ENSG00000108590	Q9Y3C7
ENSG00000110090	P50416	ENSG00000112237	P24863	ENSG00000112282	Q9ULK4
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ENSG00000118579	Q9H204	ENSG00000123066	Q71F56	ENSG00000123689	P27469
ENSG00000124151	Q9Y6Q9	ENSG00000124641	Q9H944	ENSG00000125686	Q15648
ENSG00000126368	P20393	ENSG00000130304	Q6PCB7	ENSG00000130589	Q9BYK8
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ENSG00000133398	Q9BTT4	ENSG00000133794	O00327	ENSG00000133997	O75586
ENSG00000134317	Q9NZI5	ENSG00000134852	O15516	ENSG00000135744	P01019
ENSG00000139278	P48060	ENSG00000140396	Q15596	ENSG00000140465	P04798
ENSG00000142453	Q86X55	ENSG00000143344	Q9NZL6	ENSG00000146426	Q8IVF5
ENSG00000147872	Q99541	ENSG00000151726	P33121	ENSG00000152944	Q13503
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ENSG00000161533	Q15067-1	ENSG00000161920	Q9P086	ENSG00000165029	O95477
ENSG00000167772	Q9BY76	ENSG00000167910	P22680	ENSG00000169375	Q96ST3
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ENSG00000173153	P11474	ENSG00000175221	Q9Y2X0	ENSG00000177200	Q3L8U1
ENSG00000177565	Q9BZK7	ENSG00000180182	O60244	ENSG00000184634	Q93074
ENSG00000186350	P19793	ENSG00000186951	Q07869	ENSG00000188786	Q14872
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ENSG00000281022	Q15528				

Input	Ensembl Id	Input	Ensembl Id	Input	Ensembl Id
ENSG00000005471	ENSG00000005471	ENSG00000023330	ENSG00000023330	ENSG00000065833	ENSG00000065833
ENSG00000079459	ENSG00000079459	ENSG00000101255	ENSG00000101255	ENSG00000105398	ENSG00000105398
ENSG00000110090	ENSG00000110090	ENSG00000112972	ENSG00000112972	ENSG00000115641	ENSG00000115641
ENSG00000117054	ENSG00000117054	ENSG00000123689	ENSG00000123689	ENSG00000130304	ENSG00000130304
ENSG00000134317	ENSG00000134317	ENSG00000135744	ENSG00000135744	ENSG00000139278	ENSG00000139278
ENSG00000140465	ENSG00000140465	ENSG00000143344	ENSG00000143344	ENSG00000146426	ENSG00000146426
ENSG00000147872	ENSG00000147872	ENSG00000151726	ENSG00000151726	ENSG00000157184	ENSG00000157184
ENSG00000161533	ENSG00000161533	ENSG00000165029	ENSG00000165029	ENSG00000167772	ENSG00000167772
ENSG00000167910	ENSG00000167910	ENSG00000170485	ENSG00000170485	ENSG00000186951	ENSG00000186951

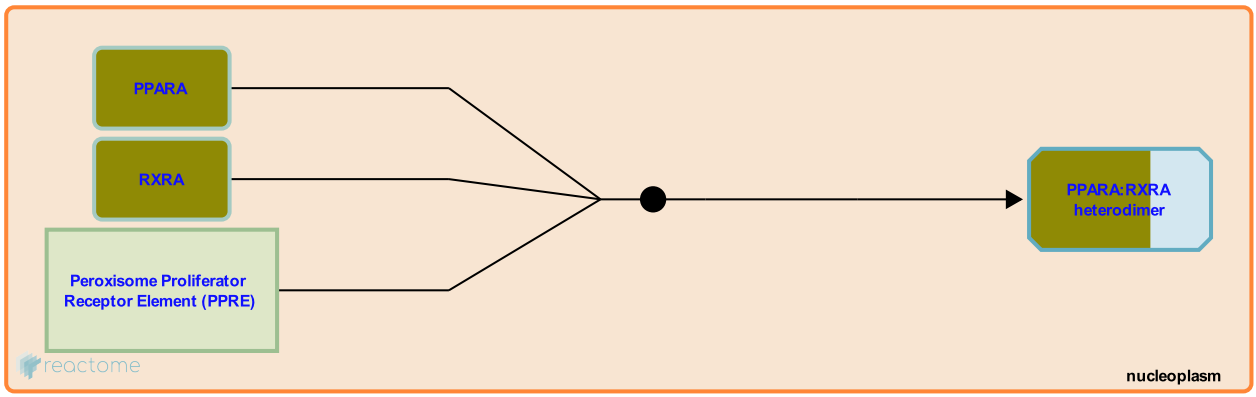
PPARA binds RXRA ↗

Location: Regulation of lipid metabolism by PPARalpha

Stable identifier: R-HSA-400204

Type: binding

Compartments: nucleoplasm



Peroxisome proliferator-activated receptor alpha (PPAR-alpha) is a type II nuclear receptor (its subcellular location is independent of ligand binding) related to PPAR-beta/delta and PPAR-gamma. PPAR-alpha is expressed highly in the liver where if functions to control lipid metabolism, especially fatty acid oxidation.
PPAR-alpha forms heterodimers with Retinoid X receptor alpha (RXR-alpha). The heterodimers bind peroxisome proliferator receptor elements (PPREs) in and around genes regulated by PPAR-alpha.

Followed by: PPARA:RXRA binds Corepressors of PPARA

Literature references

Gouni-Berthold, I., Krone, W. (2005). Peroxisome proliferator-activated receptor alpha (PPARalpha) and atherosclerosis. *Curr Drug Targets Cardiovasc Haematol Disord, 5*, 513-23. ↗

Gelman, L., Wahli, W., Michalik, L., Desvergne, B., Feige, JN. (2006). From molecular action to physiological outputs: peroxisome proliferator-activated receptors are nuclear receptors at the crossroads of key cellular functions. *Prog Lipid Res, 45*, 120-59. ↗

Green, S., Bardot, O., Aldridge, TC., Latruffe, N. (1993). PPAR-RXR heterodimer activates a peroxisome proliferator response element upstream of the bifunctional enzyme gene. *Biochem Biophys Res Commun, 192*, 37-45. ↗

Wahli, W., Desvergne, B. (1999). Peroxisome proliferator-activated receptors: nuclear control of metabolism. *Endocr Rev, 20*, 649-88. ↗

Qi, C., Reddy, JK., Zhu, Y. (2000). Peroxisome proliferator-activated receptors, coactivators, and downstream targets. *Cell Biochem Biophys, 32*, 187-204. ↗

Editions

2009-05-30	Authored, Edited	May, B.
2009-06-08	Reviewed	Kersten, S.
2009-06-08	Edited	May, B.

2 submitted entities found in this pathway, mapping to 3 Reactome entities

Input	UniProt Id	Input	UniProt Id
ENSG00000186350	P19793	ENSG00000186951	Q07869

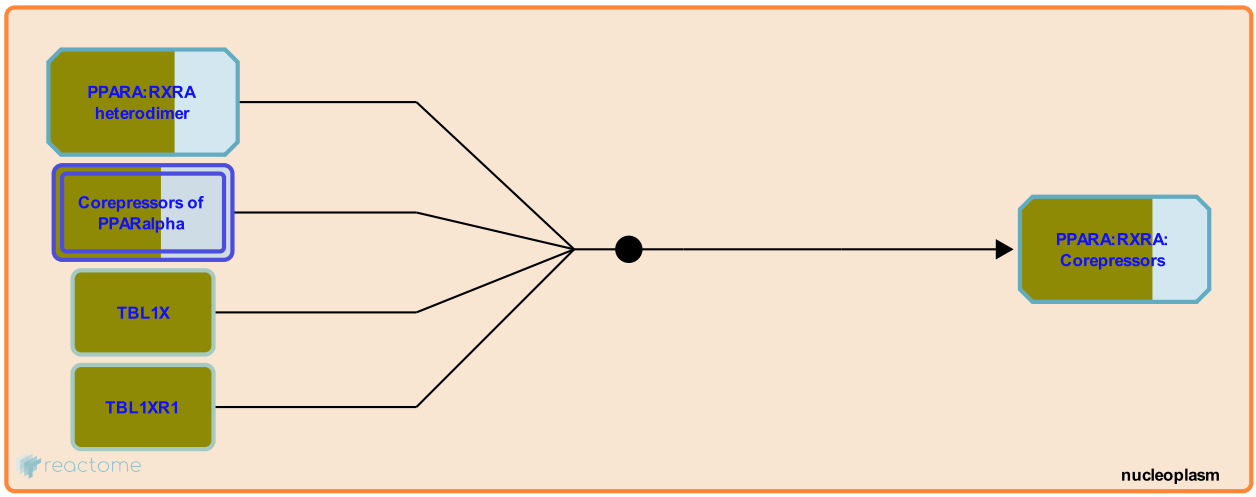
PPARA:RXRA binds Corepressors of PPARA ↗

Location: Regulation of lipid metabolism by PPARalpha

Stable identifier: R-HSA-400183

Type: binding

Compartments: nucleoplasm



In the absence of activating ligands of PPAR-alpha, the PPAR-alpha:RXR-alpha heterodimers recruit corepressors NCoR1, NCoR2(SMRT), and histone deacetylases (HDACs) to genes regulated by PPAR-alpha. The corepressors maintain chromatin at the gene in an inactive conformation and prevent expression of the gene.

Preceded by: PPARA binds RXRA

Followed by: Fatty acid ligands activate PPARA

Literature references

Gouni-Berthold, I., Krone, W. (2005). Peroxisome proliferator-activated receptor alpha (PPARalpha) and atherosclerosis. *Curr Drug Targets Cardiovasc Haematol Disord, 5*, 513-23. ↗

Gelman, L., Wahli, W., Michalik, L., Desvergne, B., Feige, JN. (2006). From molecular action to physiological outputs: peroxisome proliferator-activated receptors are nuclear receptors at the crossroads of key cellular functions. *Prog Lipid Res, 45*, 120-59. ↗

Wahli, W., Desvergne, B. (1999). Peroxisome proliferator-activated receptors: nuclear control of metabolism. *Endocr Rev, 20*, 649-88. ↗

Qi, C., Reddy, JK., Zhu, Y. (2000). Peroxisome proliferator-activated receptors, coactivators, and downstream targets. *Cell Biochem Biophys, 32*, 187-204. ↗

Kersten, S. (2008). Peroxisome proliferator activated receptors and lipoprotein metabolism. *PPAR Res, 2008*, 132960. ↗

Editions

2009-05-30	Authored, Edited	May, B.
2009-06-08	Reviewed	Kersten, S.
2009-06-08	Edited	May, B.

7 submitted entities found in this pathway, mapping to 8 Reactome entities

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
ENSG00000101849	O60907	ENSG00000169375	Q96ST3	ENSG00000171720	O15379
ENSG00000177565	Q9BZK7	ENSG00000186350	P19793	ENSG00000186951	Q07869

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
ENSG00000196498	Q9Y618				

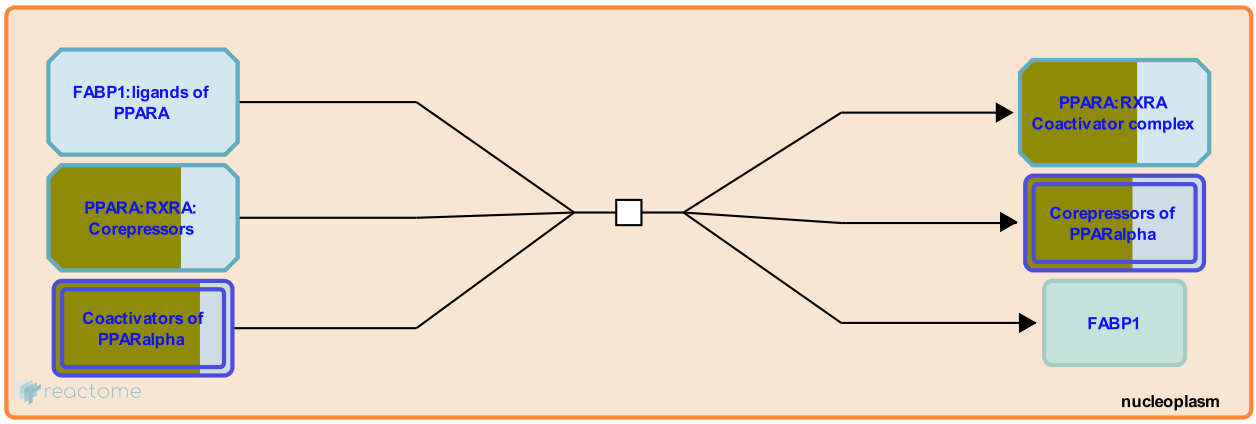
Fatty acid ligands activate PPARA ↗

Location: Regulation of lipid metabolism by PPARalpha

Stable identifier: R-HSA-400143

Type: transition

Compartments: nucleoplasm



PPAR-alpha is activated by binding polyunsaturated fatty acids especially those having 18-22 carbon groups and 2-6 double bonds. These ligands bind the C-terminal region of PPAR-alpha and include linoleic acid, linolenic acids, arachidonic acid, and eicosapentaenoic acid. The fibrate drugs are also agonists of PPAR-alpha.
Binding of a ligand causes a conformational change in PPAR-alpha so that it recruits coactivators. By analogy with the closely related receptor PPAR-gamma, PPAR-alpha probably binds TBL1 and TBLR1, which are responsible for recruiting the 19S proteasome to degrade corepressors during the exchange of corepressors for coactivators. The coactivators belong to the CBP-SRC-HAT complex (CBP/p300, SRC1, SRC2, SRC3, CARM1, SWI/SNF, BAF60C, PRIC320, and PRIC285), the ASC complex (PRIP/ASC2, PIMT), and the TRAP-DRIP-ARC-MEDIATOR complex (TRAP130, PBP/TRAP220). The coactivators contain LXXLL motifs (Nuclear Receptor Boxes) that interact with the AF-2 region in nuclear receptors such as PPAR-alpha. Additionally bilirubin binds to PPAR-alpha and acts as coactivator.

Preceded by: PPARA:RXRA binds Corepressors of PPARA

Literature references

Payne, HR., Storey, SM., Hostetler, HA., Schroeder, F., Kier, AB., McIntosh, AL. et al. (2009). L-FABP directly interacts with PPARalpha in cultured primary hepatocytes. *J Lipid Res, 50*, 1663-75. ↗

Yu, S., Reddy, JK. (2007). Transcription coactivators for peroxisome proliferator-activated receptors. *Biochim Biophys Acta, 1771*, 936-51. ↗

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Qi, C., Reddy, JK., Zhu, Y. (2000). Peroxisome proliferator-activated receptors, coactivators, and downstream targets. *Cell Biochem Biophys, 32*, 187-204. ↗

Rose, DW., Aggarwal, A., Perissi, V., Rosenfeld, MG., Glass, CK. (2004). A corepressor/coactivator exchange complex required for transcriptional activation by nuclear receptors and other regulated transcription factors. *Cell, 116*, 511-26. ↗

Editions

2009-05-30	Authored, Edited	May, B.
2009-06-08	Reviewed	Kersten, S.
2009-06-08	Edited	May, B.
2021-01-23	Reviewed	Somers, J.

16 submitted entities found in this pathway, mapping to 17 Reactome entities

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ENSG00000005339	Q92793	ENSG00000082014	Q6STE5	ENSG00000084676	Q15788
ENSG00000101849	O60907	ENSG00000125686	Q15648	ENSG00000130589	Q9BYK8
ENSG00000140396	Q15596	ENSG00000142453	Q86X55	ENSG00000169375	Q96ST3
ENSG00000171720	O15379	ENSG00000177200	Q3L8U1	ENSG00000177565	Q9BZK7
ENSG00000186350	P19793	ENSG00000186951	Q07869	ENSG00000196498	Q9Y618
ENSG00000198646	Q14686				

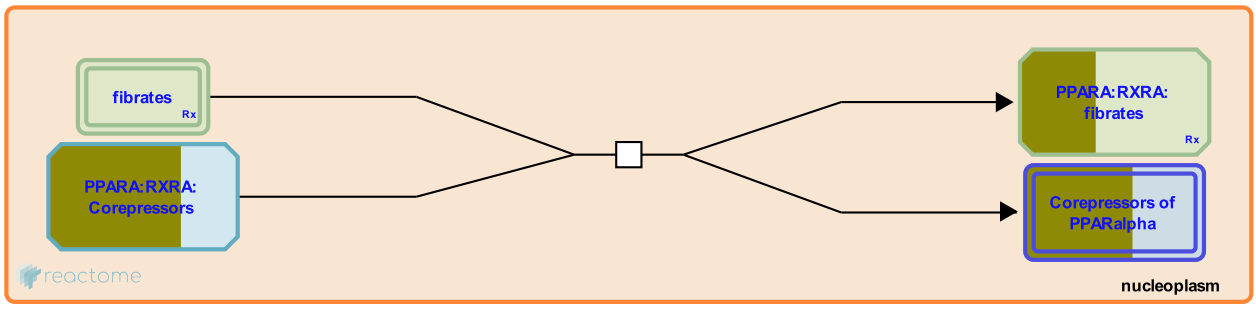
PPARA binds fibrates ↗

Location: Regulation of lipid metabolism by PPARalpha

Stable identifier: R-HSA-9734475

Type: transition

Compartments: nucleoplasm



The peroxisome proliferator-activated receptor alpha (PPARA) is a nuclear ligand-activated transcription factor that is a key regulator of fatty acid oxidation in the liver. Target genes of PPARA participate in fatty acid transport, fatty acid oxidation, triglyceride clearance, lipoprotein production, and cholesterol homeostasis. Its activation mediates lipid, glucose and amino acid homeostasis.

Fibrate drugs are derivatives of fibric acid which act as PPARA agonists and are widely used to lower triglycerides, LDL-cholesterol, total-cholesterol and apolipoprotein C3 (Grundy & Vega 1987, Clavey et al. 1999) while increasing HDL-cholesterol concentrations in serum. They are used to treat hypercholesterolemia, dyslipidemia and hypertriglyceridemia (Katsiki et al. 2013, Laufs et al. 2020). Fibrate drugs include gemfibrozil (De Filippis et al. 2011), bezafibrate (Inoue et al. 2002), cipofibrate (Quang et al. 2012), clofibrate (Henke et al. 1998) and fenofibrate (Caldwell 1989).

Literature references

Copin, C., Staels, B., Fruchart, J., Dallongeville, J., Mariotte, MC., Baugé, E. et al. (1999). Cell culture conditions determine apolipoprotein CIII secretion and regulation by fibrates in human hepatoma HepG2 cells. *Cell Physiol Biochem, 9*, 139-49. ↗

Collins, JL., Brackeen, MF., Kliewer, SA., Lehmann, JM., Blanchard, SG., Brown, KK. et al. (1998). N-(2-Benzoylphenyl)-L-tyrosine PPARgamma agonists. 1. Discovery of a novel series of potent antihyperglycemic and antihyperlipidemic agents. *J Med Chem, 41*, 5020-36. ↗

Kusama, H., Aoyagi, S., Awata, T., Hayashi, K., Katayama, S., Mastunaga, T. et al. (2002). Fibrate and statin synergistically increase the transcriptional activities of PPARalpha/RXRalpha and decrease the transactivation of NFkappaB. *Biochem Biophys Res Commun, 290*, 131-9. ↗

De Filippis, B., Maccallini, C., Fantacuzzi, M., Ammazzalorso, A., Giampietro, L., Giancristofaro, A. et al. (2011). Discovery of gemfibrozil analogues that activate PPARα and enhance the expression of gene CPT1A involved in fatty acids catabolism. *Eur J Med Chem, 46*, 5218-24. ↗

Tai, BH., Thao, NP., Quang, TH., Song, SB., Ngan, NT., Kiem, PV. et al. (2012). Anti-inflammatory and PPAR transactivational effects of secondary metabolites from the roots of Asarum sieboldii. *Bioorg Med Chem Lett, 22*, 2527-33. ↗

Editions

2021-06-17	Authored, Edited	Jassal, B.
2022-03-01	Reviewed	Huddart, R.
2022-05-10	Edited	Matthews, L.

7 submitted entities found in this pathway, mapping to 8 Reactome entities

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
ENSG00000101849	O60907	ENSG00000169375	Q96ST3	ENSG00000171720	O15379

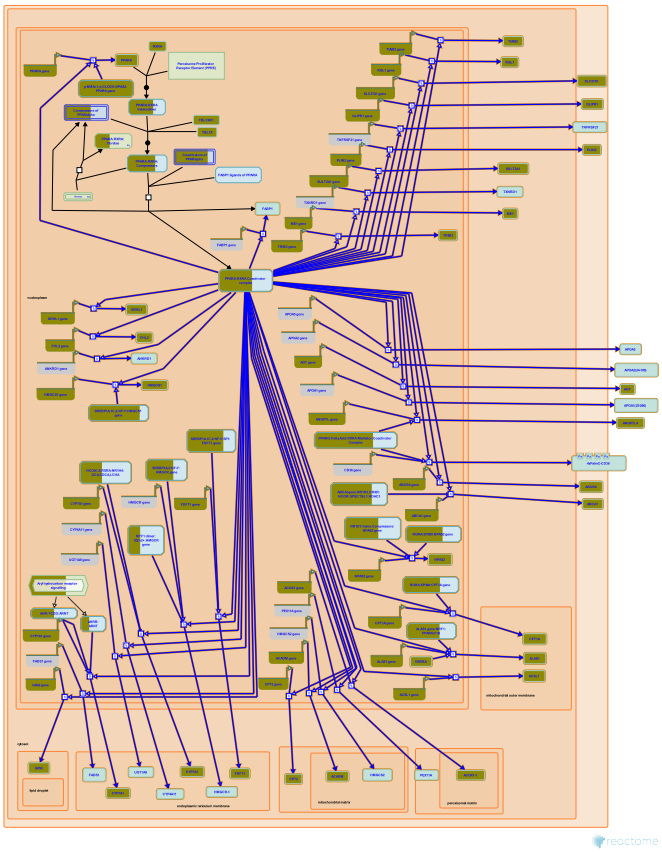
Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
ENSG00000177565	Q9BZK7	ENSG00000186350	P19793	ENSG00000186951	Q07869
ENSG00000196498	Q9Y618				

PPARA activates gene expression ↗

Location: Regulation of lipid metabolism by PPARalpha

Stable identifier: R-HSA-1989781

Compartments: peroxisomal matrix, endoplasmic reticulum membrane, plasma membrane, mitochondrial outer membrane, cytosol, mitochondrial matrix, extracellular region, lipid droplet, mitochondrial inner membrane, peroxisomal membrane, nucleoplasm



The set of genes regulated by PPAR-alpha is not fully known in humans, however many examples have been found in mice. Genes directly activated by PPAR-alpha contain peroxisome proliferator receptor elements (PPREs) in their promoters and include:
1) genes involved in fatty acid oxidation and ketogenesis (Acox1, Cyp4a, Acadm, Hmgcs2);
2) genes involved in fatty acid transport (Cd36, , Slc27a1, Fabp1, Cpt1a, Cpt2);
3) genes involved in producing fatty acids and very low density lipoproteins (Me1, Scd1);
4) genes encoding apolipoproteins (Apoa1, Apoa2, Apoa5);
5) genes involved in triglyceride clearance (Angptl4);
6) genes involved in glycerol metabolism (Gpd1 in mouse);
7) genes involved in glucose metabolism (Pdk4);
8) genes involved in peroxisome proliferation (Pex11a);
9) genes involved in lipid storage (Plin, Adfp).
Many other genes are known to be regulated by PPAR-alpha but whether their regulation is direct or indirect remains to be found. These genes include: ACACA, FAS, SREBP1, FADS1, DGAT1, ABCA1, PLTP, ABCB4, UGT2B4, SULT2A1, Pnpla2, Acsl1, Slc27a4, many Acot genes, and others (reviewed in Rakhshandehroo et al. 2010).

Literature references

Mandard, S., Kersten, S., Muller, M. (2004). Peroxisome proliferator-activated receptor alpha target genes. *Cell Mol Life Sci, 61*, 393-416. ↗

Wahli, W., Desvergne, B. (1999). Peroxisome proliferator-activated receptors: nuclear control of metabolism. *Endocr Rev, 20*, 649-88. ↗

Kersten, S., Knoch, B., Rakhshandehroo, M., Müller, M. (2010). Peroxisome proliferator-activated receptor alpha target genes. *PPAR Res, 2010*. ↗

Qi, C., Reddy, JK., Zhu, Y. (2000). Peroxisome proliferator-activated receptors, coactivators, and downstream targets. *Cell Biochem Biophys, 32*, 187-204. ↗

Kersten, S. (2008). Peroxisome proliferator activated receptors and lipoprotein metabolism. *PPAR Res, 2008*, 132960. ↗

Editions

2009-06-08	Reviewed	Kersten, S.
2011-11-08	Authored, Edited	May, B.

81 submitted entities found in this pathway, mapping to 109 Reactome entities

Input	UniProt Id	Input	UniProt Id	Input	UniProt Id
ENSG00000001167	P23511	ENSG00000005339	Q92793	ENSG00000005471	P21439
ENSG00000008838	O75448	ENSG00000023330	P13196	ENSG00000025434	Q13133
ENSG00000042429	Q9NVC6	ENSG00000063322	Q9NX70	ENSG00000065833	P48163
ENSG00000066136	Q13952	ENSG00000072310	P36956-1, P36956-3	ENSG00000079459	P37268
ENSG00000082014	Q6STE5	ENSG00000084676	Q15788	ENSG00000099917	Q96RN5
ENSG00000100393	Q09472	ENSG00000101255	Q96RU7	ENSG00000101849	O60907
ENSG00000104973	Q71SY5	ENSG00000105085	O95402	ENSG00000105398	Q06520
ENSG00000106546	P35869	ENSG00000108510	Q9UHV7	ENSG00000108590	Q9Y3C7
ENSG00000110090	P50416	ENSG00000112237	P24863	ENSG00000112282	Q9ULK4
ENSG00000112972	Q01581	ENSG00000115641	Q14192	ENSG00000117054	P11310
ENSG00000118579	Q9H204	ENSG00000123066	Q71F56	ENSG00000123689	P27469
ENSG00000124151	Q9Y6Q9	ENSG00000124641	Q9H944	ENSG00000125686	Q15648
ENSG00000126368	P20393	ENSG00000130304	Q6PCB7	ENSG00000130589	Q9BYK8
ENSG00000130772	Q9BUE0	ENSG00000131408	P55055	ENSG00000132964	P49336
ENSG00000133398	Q9BTT4	ENSG00000133794	O00327	ENSG00000133997	O75586
ENSG00000134317	Q9NZI5	ENSG00000134852	O15516	ENSG00000135744	P01019
ENSG00000139278	P48060	ENSG00000140396	Q15596	ENSG00000140465	P04798
ENSG00000142453	Q86X55	ENSG00000143344	Q9NZL6	ENSG00000146426	Q8IVF5
ENSG00000147872	Q99541	ENSG00000151726	P33121	ENSG00000152944	Q13503
ENSG00000155846	Q86YN6	ENSG00000157184	P23786	ENSG00000160563	Q6P2C8
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ENSG00000167772	Q9BY76	ENSG00000167910	P22680	ENSG00000170485	Q99743
ENSG00000171720	O15379	ENSG00000172379	Q9HBZ2	ENSG00000173153	P11474
ENSG00000175221	Q9Y2X0	ENSG00000177200	Q3L8U1	ENSG00000177565	Q9BZK7
ENSG00000180182	O60244	ENSG00000184634	Q93074	ENSG00000186350	P19793
ENSG00000186951	Q07869	ENSG00000188786	Q14872	ENSG00000196498	Q9Y618
ENSG00000198646	Q14686	ENSG00000198911	Q12772	ENSG00000281022	Q15528

Input	Ensembl Id	Input	Ensembl Id	Input	Ensembl Id
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ENSG00000110090	ENSG00000110090	ENSG00000112972	ENSG00000112972	ENSG00000115641	ENSG00000115641
ENSG00000117054	ENSG00000117054	ENSG00000123689	ENSG00000123689	ENSG00000130304	ENSG00000130304
ENSG00000134317	ENSG00000134317	ENSG00000135744	ENSG00000135744	ENSG00000139278	ENSG00000139278
ENSG00000140465	ENSG00000140465	ENSG00000143344	ENSG00000143344	ENSG00000146426	ENSG00000146426
ENSG00000147872	ENSG00000147872	ENSG00000151726	ENSG00000151726	ENSG00000157184	ENSG00000157184
ENSG00000161533	ENSG00000161533	ENSG00000165029	ENSG00000165029	ENSG00000167772	ENSG00000167772

Input	Ensembl Id	Input	Ensembl Id	Input	Ensembl Id
ENSG00000167910	ENSG00000167910	ENSG00000170485	ENSG00000170485	ENSG00000186951	ENSG00000186951

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