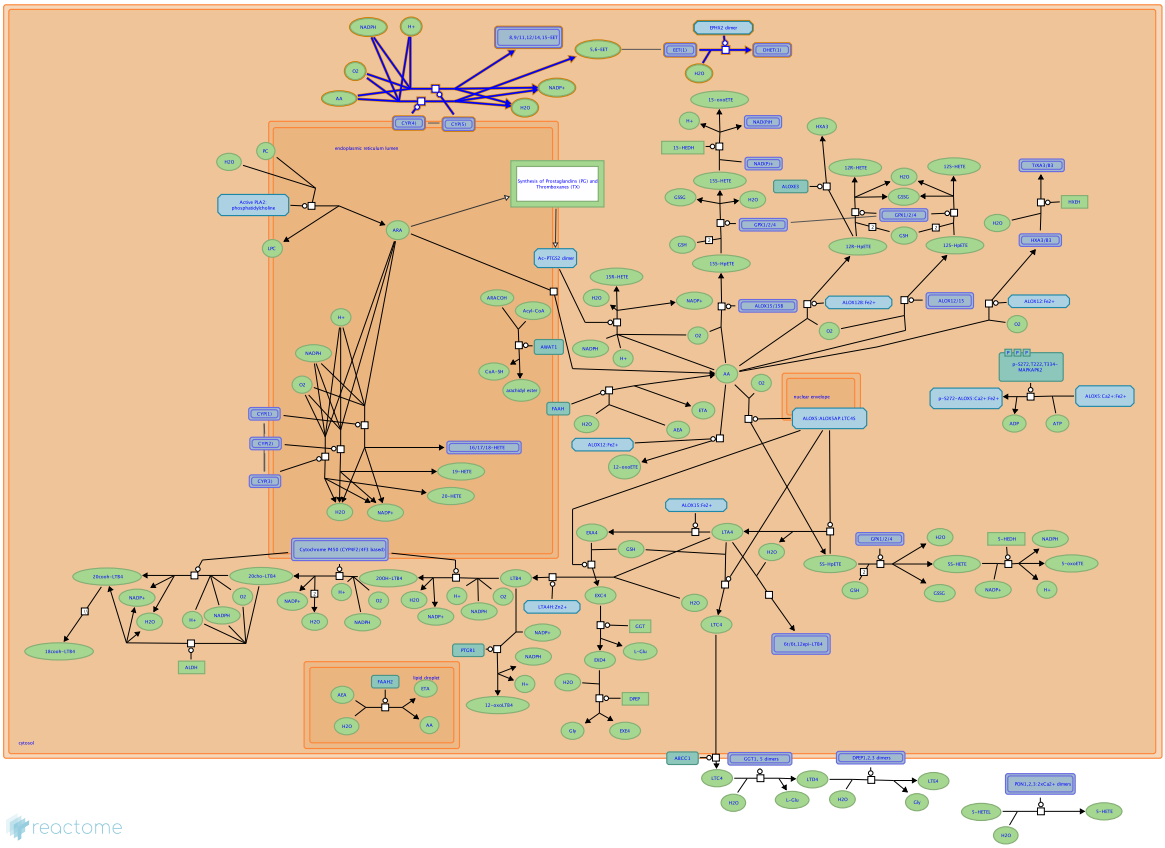
Synthesis of epoxy (EET) and di-hydroxyeicosatrienoic acids (DHET)



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30/09/2021

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.

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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. ↗

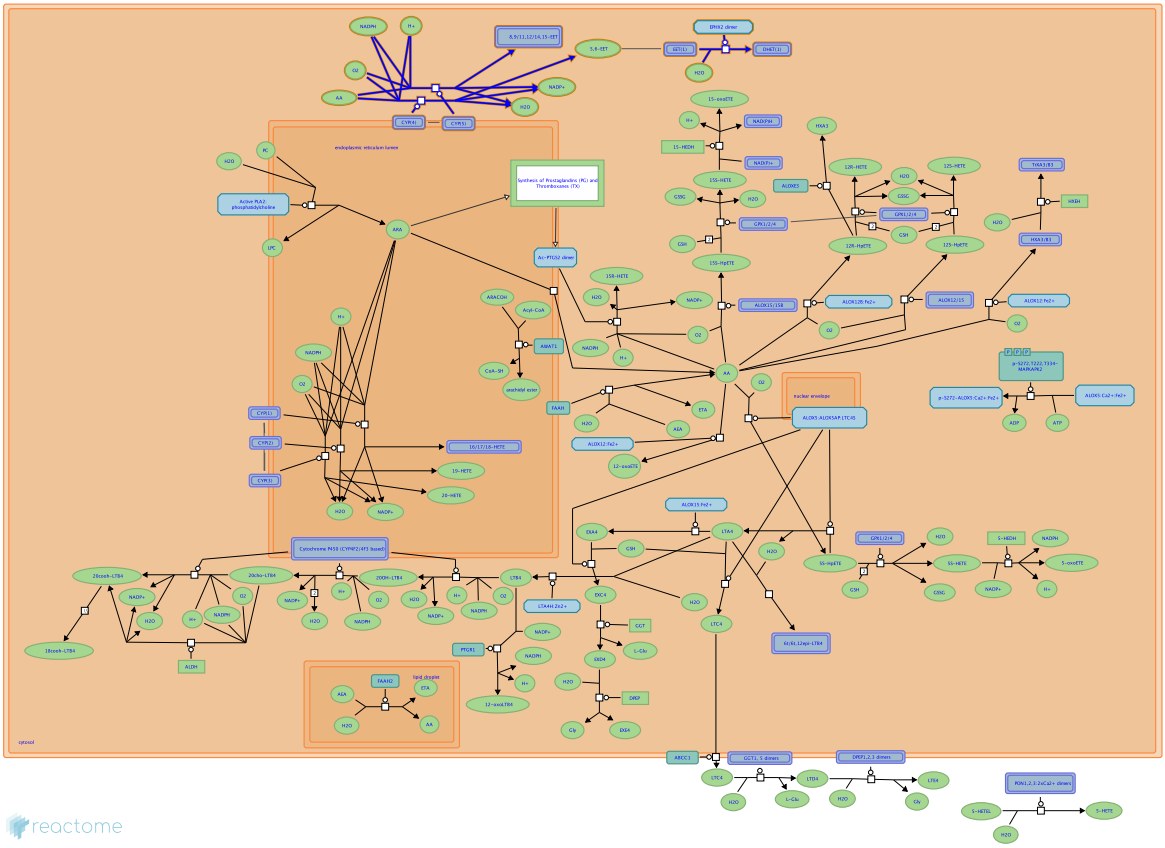
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Synthesis of epoxy (EET) and dihydroxyeicosatrienoic acids (DHET) ↗

Stable identifier: R-HSA-2142670



The epoxidation of arachidonic acid by cytochrome P450s (CYPs) results in the formation of unique bioactive lipid mediators termed epoxyeicosatrienoic acids (EETs). Each double bond has been shown to be susceptible to oxidation, resulting in 5,6-EET, 8,9-EET, 11,12-EET, and 14,15-EET. The majority of the EET biological activities are diminished by the hydrolysis to the corresponding dihydroxyeicosatrienoic acids (DHET) (Capdevila et al. 2000, Buczynski et al. 2009, Vance & Vance 2008).

Literature references

Vance, DE., Vance, JE. (2008). The eicosanoids: cyclooxygenase, lipoxygenase, and epoxygenase pathways, Biochemistry of Lipids, Lipoproteins and Membranes, 5th Edition. *Elsevier Science*, 331-362.

Buczynski, MW., Dumlao, DS., Dennis, EA. (2009). Thematic Review Series: Proteomics. An integrated omics analysis of eicosanoid biology. *J Lipid Res, 50*, 1015-38. ↗

Capdevila, JH., Falck, JR., Harris, RC. (2000). Cytochrome P450 and arachidonic acid bioactivation. Molecular and functional properties of the arachidonate monooxygenase. *J Lipid Res, 41*, 163-81. ↗

Editions

2012-02-24	Authored, Edited	Williams, MG.
2012-11-10	Reviewed	Rush, MG.

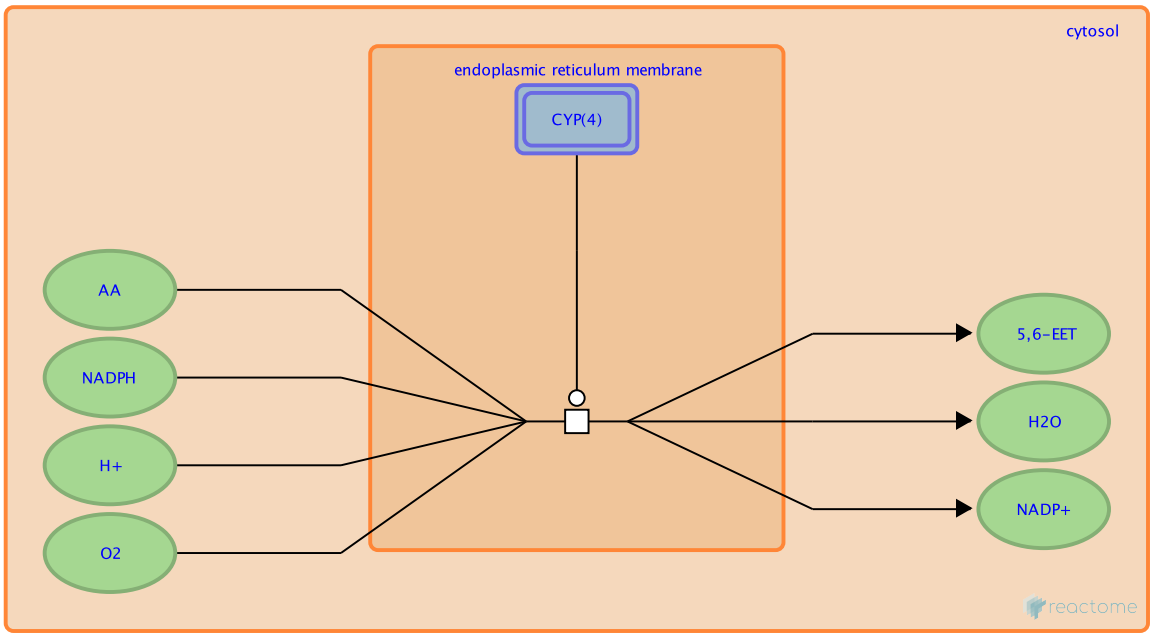
Arachidonic acid is epoxidated to 5,6-EET by CYP(4) ↗

Location: Synthesis of epoxy (EET) and dihydroxyeicosatrienoic acids (DHET)

Stable identifier: R-HSA-2161890

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



Several cytochrome P450s (CYPs) convert arachidonic acid to 5,6-epoxyeicosatrienoic acid (5,6-EET). The CYPs and their references are as follows: CYP1A1, CYP1A2, CYP1B1 (Choudhary et al. 2004); CYP2J2 (Wu et al. 1996).

Followed by: EET(1) is hydrolysed to DHET(1) by EPHX2

Literature references

Choudhary, D., Jansson, I., Stoilov, I., Sarfarazi, M., Schenkman, JB. (2004). Metabolism of retinoids and arachidonic acid by human and mouse cytochrome P450 1b1. *Drug Metab Dispos, 32*, 840-7. ↗

Wu, S., Moomaw, CR., Tomer, KB., Falck, JR., Zeldin, DC. (1996). Molecular cloning and expression of CYP2J2, a human cytochrome P450 arachidonic acid epoxygenase highly expressed in heart. *J Biol Chem, 271*, 3460-8. ↗

Editions

2012-02-24	Authored, Edited	Williams, MG.
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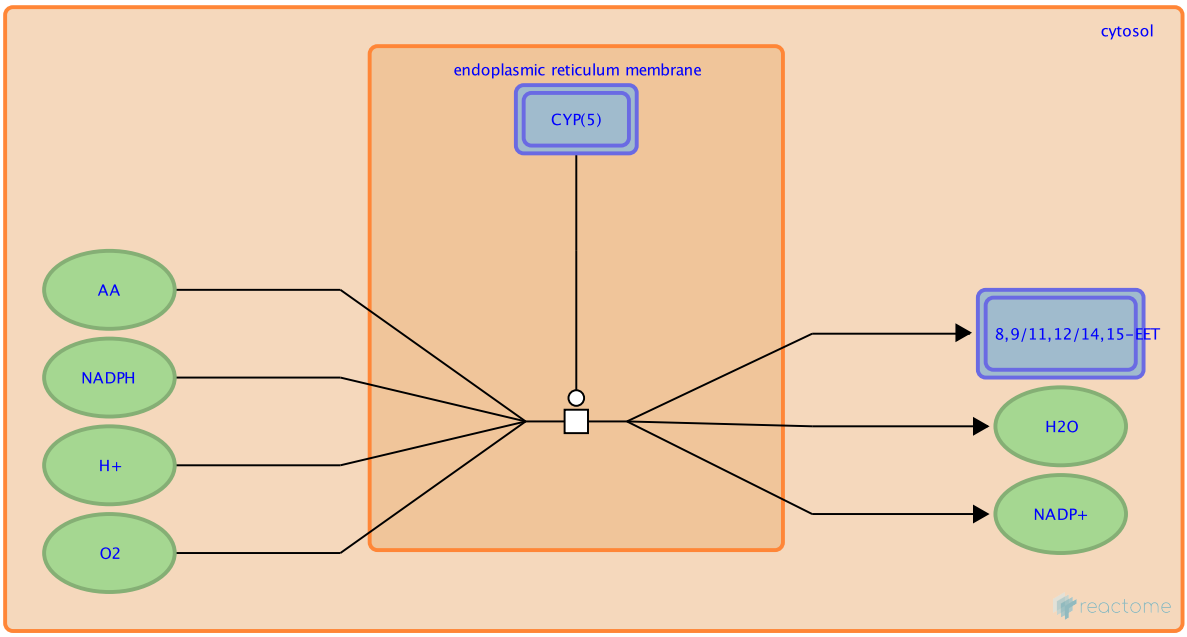
Arachidonic acid is epoxidated to 8,9/11,12/14,15-EET by CYP(5) ↗

Location: Synthesis of epoxy (EET) and dihydroxyeicosatrienoic acids (DHET)

Stable identifier: R-HSA-2161899

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol



Several cytochrome P450s (CYPs) convert arachidonic acid to 8,9-, 11,12-, and 14,15-epoxyeicosatrienoic acids (8,9-, 11,12-, 14,15-EETs). The CYPs and their references are as follows: CYP1A1, CYP1A2, CYP1B1 (Choudhary et al. 2004); CYP2C8, CYP2C9 (Rifkind et al. 1995); CYP2C19 (Bylund et al. 1998, Rifkind et al. 1995); CYP2J2 (Wu et al. 1996).

Followed by: EET(1) is hydrolysed to DHET(1) by EPHX2

Literature references

Choudhary, D., Jansson, I., Stoilov, I., Sarfarazi, M., Schenkman, JB. (2004). Metabolism of retinoids and arachidonic acid by human and mouse cytochrome P450 1b1. *Drug Metab Dispos, 32*, 840-7. ↗

Bylund, J., Ericsson, J., Oliw, EH. (1998). Analysis of cytochrome P450 metabolites of arachidonic and linoleic acids by liquid chromatography-mass spectrometry with ion trap MS. *Anal Biochem, 265*, 55-68. ↗

Rifkind, AB., Lee, C., Chang, TK., Waxman, DJ. (1995). Arachidonic acid metabolism by human cytochrome P450s 2C8, 2C9, 2E1, and 1A2: regioselective oxygenation and evidence for a role for CYP2C enzymes in arachidonic acid epoxygenation in human liver microsomes. *Arch Biochem Biophys, 320*, 380-9. ↗

Wu, S., Moomaw, CR., Tomer, KB., Falck, JR., Zeldin, DC. (1996). Molecular cloning and expression of CYP2J2, a human cytochrome P450 arachidonic acid epoxygenase highly expressed in heart. *J Biol Chem, 271*, 3460-8. ↗

Editions

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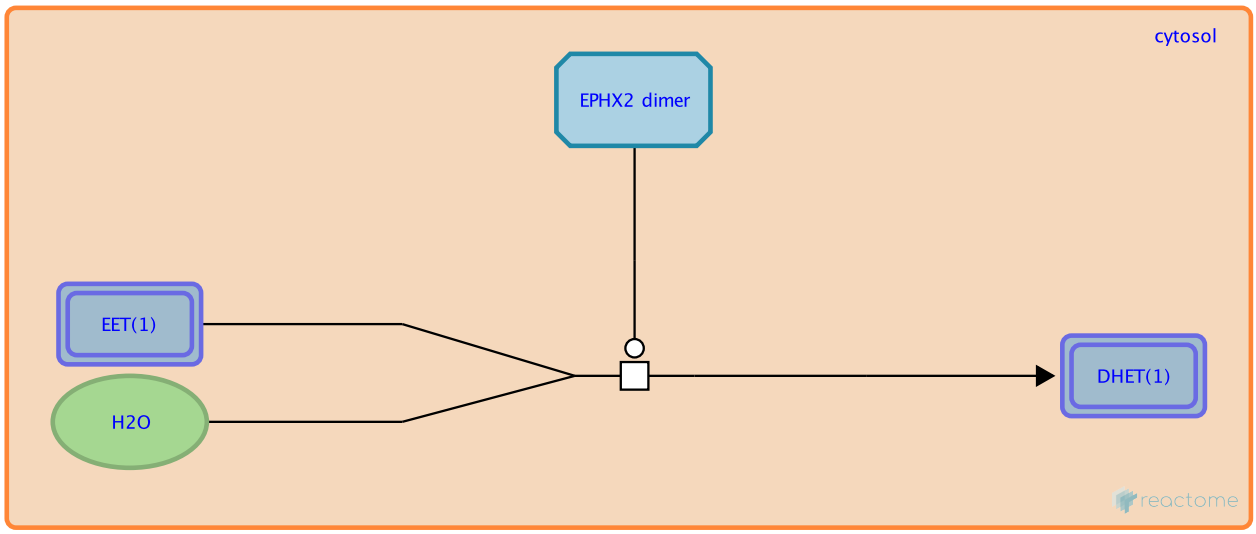
EET(1) is hydrolysed to DHET(1) by EPHX2 ↗

Location: Synthesis of epoxy (EET) and dihydroxyeicosatrienoic acids (DHET)

Stable identifier: R-HSA-2161961

Type: transition

Compartments: cytosol



Epoxide hydrolase 2 (EPHX2) hydrolyses 5,6-, 8,9-, 11,12-, and 14,15-epoxyeicosatrienoic acids ("EET(1)") to their corresponding dihydroxyeicosatrienoic acids ("DHET(1)") (Werner et al. 2002; Gomez et al. 2004). The majority of the EET biological activities are diminished by this hydrolysis.

Preceded by: Arachidonic acid is epoxidated to 5,6-EET by CYP(4), Arachidonic acid is epoxidated to 8,9/11,12/14,15-EET by CYP(5)

Literature references

Werner, K., Schaefer, WR., Schweer, H., Deppert, WR., Karck, U., Zahradnik, HP. (2002). Characterization and identification of cytochrome P450 metabolites of arachidonic acid released by human peritoneal macrophages obtained from the pouch of Douglas. *Prostaglandins Leukot Essent Fatty Acids, 67*, 397-404. ↗

Gomez, GA., Morisseau, C., Hammock, BD., Christianson, DW. (2004). Structure of human epoxide hydrolase reveals mechanistic inferences on bifunctional catalysis in epoxide and phosphate ester hydrolysis. *Biochemistry, 43*, 4716-23. ↗

Editions

2012-02-24	Authored, Edited	Williams, MG.
2012-11-10	Reviewed	Rush, MG.

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