Fatty acids

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02/08/2020
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


Reactome database release: 73

This document contains 1 pathway and 4 reactions (see Table of Contents)
**Fatty acids**

**Stable identifier:** R-HSA-211935

**Compartments:** endoplasmic reticulum membrane, endoplasmic reticulum lumen

The CYP4 family are the main CYPs involved in the metabolism of long-chain fatty acids.

**Literature references**


**Editions**

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CYP2J2 oxidises ARA

**Location:** Fatty acids

**Stable identifier:** R-HSA-211983

**Type:** transition

**Compartments:** smooth endoplasmic reticulum

Activation of phospholipases releases free arachidonic acid (ARA) from phospholipid bilayers which can then be metabolised to biologically active eicosanoids (signaling molecules which exert effects in inflammation and immunity). The cytochrome P450 enzyme CYP2J2 (arachidonic acid epoxygenase) is mainly expressed in human heart and can metabolise ARA to epoxyeicosatrienoic acid (EET). Four cis-EETs can be produced: 5,6-, 8,9-, 11,12- and 14,15-EET. Each of these can be formed as the R,S or the S,R enantiomer (Zeldin DC, 2001). The most abundant regioisomer in human heart is 14,15-EET although 11,12-EET possesses the most potent anti-inflammatory effect (Wu et al. 1996).

**Literature references**


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CYP4A11 12-hydroxylates DDCX

**Location:** Fatty acids

**Stable identifier:** R-HSA-76466

**Type:** transition

**Compartments:** smooth endoplasmic reticulum

Dodecanoic acid (DDCX aka lauric acid) is a medium-chain fatty acid which serves as a model substrate for studying the CYP4A gene subfamily of cytochrome P450s. CYP4A11 and CYP2E1 are the principal isozymes involved in omega-hydroxylation and omega-1 hydroxylation respectively of DDCX.

**Literature references**


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CYP4B1 12-hydroxylates ARA

**Location:** Fatty acids

**Stable identifier:** R-HSA-211924

**Type:** transition

**Compartments:** smooth endoplasmic reticulum

Injury to the eye's surface provokes an inflammatory response, mediated, in part, by 12-hydroxyeicosanoids. CYP4B1 catalyses the 12-hydroxylation of arachidonic acid (ARA) to 12-HETE and 12-HETrE (12-hydroxy-5,8,10,14-eicosatetraenoic acid and 12-hydroxy-5,8,14-eicosatrienoic acid respectively). Both these metabolites possess potent inflammatory and angiogenic properties (Ashkar et al. 2004). The example of 12-HETE formation only is shown here.

**Literature references**


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CYP4F12 18-hydroxylates ARA

**Location:** Fatty acids

**Stable identifier:** R-HSA-211904

**Type:** transition

**Compartments:** smooth endoplasmic reticulum

Human CYP4F12 is involved in metabolism of endogenous compounds such as inflammatory mediators (arachidonic acid and prostaglandin H2) as well as xenobiotics like terfenadine (an antihistaminic drug) (Bylund et al. 2001). The omega-hydroxylation of arachidonic acid (ARA) is shown here to form 18-hydroxyarachidonic acid (18OH-ARA aka 18-HETE).

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