Synthesis of 12-eicosatetraenoic acid derivatives

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04/07/2022
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: 81

This document contains 1 pathway and 6 reactions (see Table of Contents)
Synthesis of 12-eicosatetraenoic acid derivatives

Stable identifier: R-HSA-2142712

The 12-eicosatetraenoic acids: 12-hydroperoxy-eicosatetraenoic acid (12-HpETE), 12-hydroxyeicosatetraenoic acid (12-HETE) and 12-oxo-eicosatetraenoic acid (12-oxoETE) are formed after the initial step of arachidonic acid oxidation by the arachidonate 12 and 15 lipoxygenases (ALOX12, ALOX12B and ALOX15 respectively). This part of the pathway is bifurcated at the level of 12S-hydroperoxy-eicosatetraenoic acid (12S-HpETE), which can either be reduced to 12S-hydro-eicosatetraenoic acid (12S-HETE) or converted to hepoxilins (Buczynski et al. 2009, Vance & Vance 2008).

Literature references


Editions

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Arachidonic acid is oxidised to 12R-HpETE by ALOX12B

Location: Synthesis of 12-eicosatetraenoic acid derivatives

Stable identifier: R-HSA-2161950

Type: transition

Compartments: cytosol

The arachidonate 12-lipoxygenase, 12R-type (ALOX12B) oxidises arachidonic acid to 12R-hydroperoxy-eicosatetraenoic acid (12R-HpETE) (Boeglin et al. 1998).

Followed by: ALOXE3 isomerises 12R-HpETE to HXA3, 12R-HpETE is reduced to 12R-HETE by GPX1/2/4

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12R-HpETE is reduced to 12R-HETE by GPX1/2/4

**Location:** Synthesis of 12-eicosatetraenoic acid derivatives

**Stable identifier:** R-HSA-2161959

**Type:** transition

**Compartments:** cytosol

Glutathione peroxidase 1 (GPX1) (Bryant et al. 1982, Sutherland et al. 2001), 2 (GPX2) (Chu et al. 1993), and 4 (Bryant et al. 1982, Sutherland et al. 2001) are involved in converting 12R-hydroperoxy-eicosatetraenoic acid (12R-HpETE) to 12R-hydro-eicosatetraenoic acid (12R-HETE).

**Preceded by:** Arachidonic acid is oxidised to 12R-HpETE by ALOX12B

**Literature references**


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**ALOXE3 isomerises 12R-HpETE to HXA3**

**Location:** Synthesis of 12-eicosatetraenoic acid derivatives

**Stable identifier:** R-HSA-8942208

**Type:** transition

**Compartments:** cytosol

Hydroperoxide isomerase (ALOXE3, e-LOX-3) is a non-heme iron-containing lipoxygenase which is atypical in that it displays a prominent hydroperoxide isomerase activity and a reduced dioxygenase activity compared to other lipoxygenases. The hydroperoxide isomerase activity catalyses the isomerisation of hydroperoxides, derived from arachidonic and linoleic acid by ALOX12B, into epoxyalcohols (Yu et al. 2003).

In the skin, ALOXE3 acts downstream of ALOX12B on the linoleate moiety of esterified omega-hydroxy-acyl-sphingosine (EOS) ceramides to produce an epoxy-ketone derivative, a crucial step in the conjugation of omega-hydroxyceramide to membrane proteins, important for the maintenance of the skin permeability barrier and protection against water loss. Loss-of-function mutations in ALOX12B and ALOXE3 represent the second most common cause of autosomal recessive congenital ichthyosis, a hereditary disorder of keratinization (Yu et al. 2005, Wang et al. 2015). Targeted disruption of these genes in mice resulted in neonatal death due to a severely impaired permeability barrier function (Zheng et al. 2011).

**Preceded by:** Arachidonic acid is oxidised to 12R-HpETE by ALOX12B

**Literature references**


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Arachidonic acid is oxidised to 12S-HpETE by ALOX12/15

Location: Synthesis of 12-eicosatetraenoic acid derivatives

Stable identifier: R-HSA-2161964

Type: transition

Compartments: cytosol


Followed by: 12S-HpETE is reduced to 12S-HETE by GPX1/2/4

Literature references


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12S-HpETE is reduced to 12S-HETE by GPX1/2/4

**Location:** Synthesis of 12-eicosatetraenoic acid derivatives

**Stable identifier:** R-HSA-2161999

**Type:** transition

**Compartments:** cytosol

Glutathione peroxidase 1 (GPX1) (Bryant et al. 1982, Sutherland et al. 2001), 2 (GPX2) (Chu et al. 1993), and 4 (Bryant et al. 1982, Sutherland et al. 2001) are involved in converting 12S-hydroperoxy-eicosatetraenoic acid (12S-HpETE) to 12S-hydro-eicosatetraenoic acid (12S-HETE). GPXs are selenoenzymes that are responsible for reducing the cellular peroxide. Cellular GPXs compete with hepoxilins A3 (HXA3) synthase for 12S-HpETE as substrate either to produce 12S-HETE or to convert to HXA3, respectively.

**Preceded by:** Arachidonic acid is oxidised to 12S-HpETE by ALOX12/15

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Arachidonic acid is converted to 12-oxoETE by ALOX12↗

**Location:** Synthesis of 12-eicosatetraenoic acid derivatives

**Stable identifier:** R-HSA-2161948

**Type:** transition

**Compartments:** cytosol

Arachidonate 12-lipoxygenase, 12S-type (ALOX12) catalyses the formation of 12-oxo-eicosatetraenoic acid (12-oxoETE) from arachidonic acid. This conversion has been observed when normal human epidermis is exposed to arachidonic acid and with the purified recombinant enzyme in vitro (Anton & Vila 2000).

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- ALOXE3 isomerises 12R-HpETE to HXA3
- Arachidonic acid is oxidised to 12S-HpETE by ALOX12/15
- 12S-HpETE is reduced to 12S-HETE by GPX1/2/4
- Arachidonic acid is converted to 12-oxoETE by ALOX12