Biosynthesis of DPAn-3 SPMs

Hansen, TV., Jassal, B.

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

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20/05/2019
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: 68

This document contains 4 pathways and 1 reaction (see Table of Contents)
**Biosynthesis of DPAn-3 SPMs**

**Stable identifier:** R-HSA-9025094

The polyunsaturated fatty acid (PUFA) ω-3 cis-7,10,13,16,19-docosapentaenoic acid (DPAn-3) is an intermediate in the biosynthesis of docosahexaenoic acid (DHA) from eicosapentaenoic acid (EPA) and is also a precursor for the production of novel bioactive mediators. The proposed biosynthesis of specialised proresolving mediators (SPMs) derived from DPAn-3 is described here (Dalli et al. 2013, Hansen et al. 2017, Vik et al. 2017). The products of the ω-3 isomer were characterised based on DHA (docosahexaenoic acid) derived resolvins, protectins and maresins (Serhan et al. 2002, Bannenberg & Serhan 2010). The same biosynthetic route as DHA-derived SPMs is probably how DPAn-3 products are also formed (Dalli et al. 2013).

**Literature references**


**Editions**

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https://reactome.org
PTGS2 dimer oxidises DPAn-3 to 13(R)-HDPAn-3

Location: Biosynthesis of DPAn-3 SPMs

Stable identifier: R-HSA-9026408

Type: transition

Compartments: cytosol, endoplasmic reticulum membrane

Incubation of ω-3 docosapentaenoic acid (DPAn-3) with human recombinant cyclooxygenase 2 (PTGS2 dimer, COX2) in vascular endothelial cells produces 13(R)-hydroxy-docasapentaenoic acid (13(R)-HDPAn-3), the precursor of 13(R)-resolvins and the electrophilic 13-oxo-DPAn-3 (Dalli et al. 2015, Primdahl et al. 2016).

Literature references


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Biosynthesis of DPAn-3-derived protectins and resolvins

Location: Biosynthesis of DPAn-3 SPMs

Stable identifier: R-HSA-9026286

The polyunsaturated fatty acid (PUFA) ω-3 cis-7,10,13,16,19-docosapentaenoic acid (DPAn-3) is an intermediate in the biosynthesis of docosahexaenoic acid (DHA) from eicosapentaenoic acid (EPA) and is also a precursor for the production of novel bioactive mediators. The proposed biosynthesis of resolvins and protectins derived from DPAn-3 is described here (Dalli et al. 2013, Hansen et al. 2017, Vik et al. 2017). 15-lipoxygenase oxygenates DPAn-3 to its 17(S) hydroperoxy epimer from which resolvins and protectins are formed via a combination of oxygenation, reduction and hydrolysis reactions (Dalli et al. 2013). The products of the ω-3 isomer were characterised based on docosahexaenoic acid (DHA)-derived resolvins and protectins (Serhan et al. 2002) and were demonstrated to have similar potent systemic anti-inflammatory and tissue protective actions as DHA-derived specialised proresolving mediators (SPMs) (Dalli et al. 2013). The same biosynthetic route as DHA-derived SPMs is probably how DPAn-3 products are also formed (Dalli et al. 2013).

Literature references


Hansen, TV., Dalli, J., Serhan, CN. (2017). The novel lipid mediator PD1n-3 DPA: An overview of the structural elucidation, synthesis, biosynthesis and bioactions. Prostaglandins Other Lipid Mediat..
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The polyunsaturated fatty acid (PUFA) ω-3 cis-7,10,13,16,19-docosapentaenoic acid (DPAn-3) is an intermediate in the biosynthesis of docosahexaenoic acid (DHA) from eicosapentaenoic acid (EPA) and is also a precursor for the production of novel bioactive mediators. The proposed biosynthesis of maresins derived from DPAn-3 is described here (Dalli et al. 2013, Hansen et al. 2017, Vik et al. 2017). 12-lipoxygenase oxygenates DPAn-3 to its 14(S) hydroperoxy epimer from which maresins are formed via a combination of oxygenation, reduction and hydrolysis reactions (Dalli et al. 2013). The products of the ω-3 isomer were characterised based on docosahexaenoic acid (DHA)-derived maresins (Serhan et al. 2015) and were demonstrated to have similar potent systemic anti-inflammatory and tissue protective actions as DHA-derived specialised proresolving mediators (SPMs) (Dalli et al. 2013). The same biosynthetic route as DHA-derived SPMs is probably how DPAn-3 products are also formed (Dalli et al. 2013).

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Biosynthesis of DPAn-3-derived 13-series resolvins

Location: Biosynthesis of DPAn-3 SPMs

Stable identifier: R-HSA-9026403

Neutrophils adherence to the vascular endothelium is a critical and early event in the innate immune response to injury or invading pathogens (Sadik et al. 2011). Studies of the lipid fraction from neutrophil-endothelial cell cultures resulted in the discovery of four novel specialised proresolving mediators (SPMs) (Dalli et al. 2015). Results from LC/MS-MS metabololipidomics using a chemically-synthesised precursor (13(R)-hydroxy-DPAn-3) identified four mediators generated from this precursor.

The polyunsaturated fatty acid (PUFA) ω-3 cis-7,10,13,16,19-docosapentaenoic acid (DPAn-3) is an intermediate in the biosynthesis of docosahexaenoic acid (DHA) from eicosapentaenoic acid (EPA) and is also a precursor for the production of novel bioactive mediators. DPAn-3 can form this precursor when acted upon by cyclooxygenase 2 (COX2). Thus these novel 13-series resolvins (RvT1-4) originate from DPAn-3 (Primdahl et al. 2016). In E. coli-infected mice, RvTs accelerated resolution of inflammation and increased survival. RvTs also regulated human and mouse phagocyte responses, stimulating bacterial phagocytosis and regulating inflammasome components (Dalli et al. 2015). The biosynthetic routes of these RvTs are described here. RvT formation requires neutrophil-endothelial cell interaction and is thought to proceed via a two-step process; COX2 hydroxylates DPAn-3 to 13(R)-DPAn-3 which trafficks to adjacent neutrophils where it is lipoxygenated by 5-lipoxygenase to RvT1-4 (Vik et al. 2017).

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