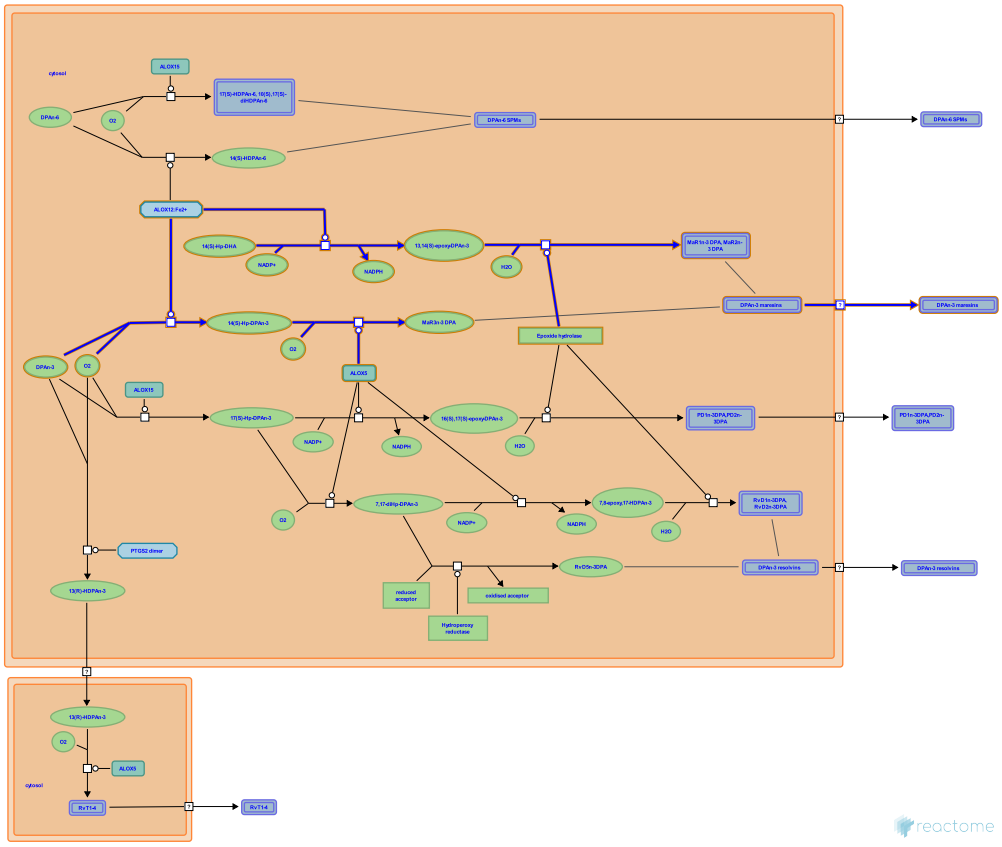
Biosynthesis of DPAn-3-derived maresins



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

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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. ↗

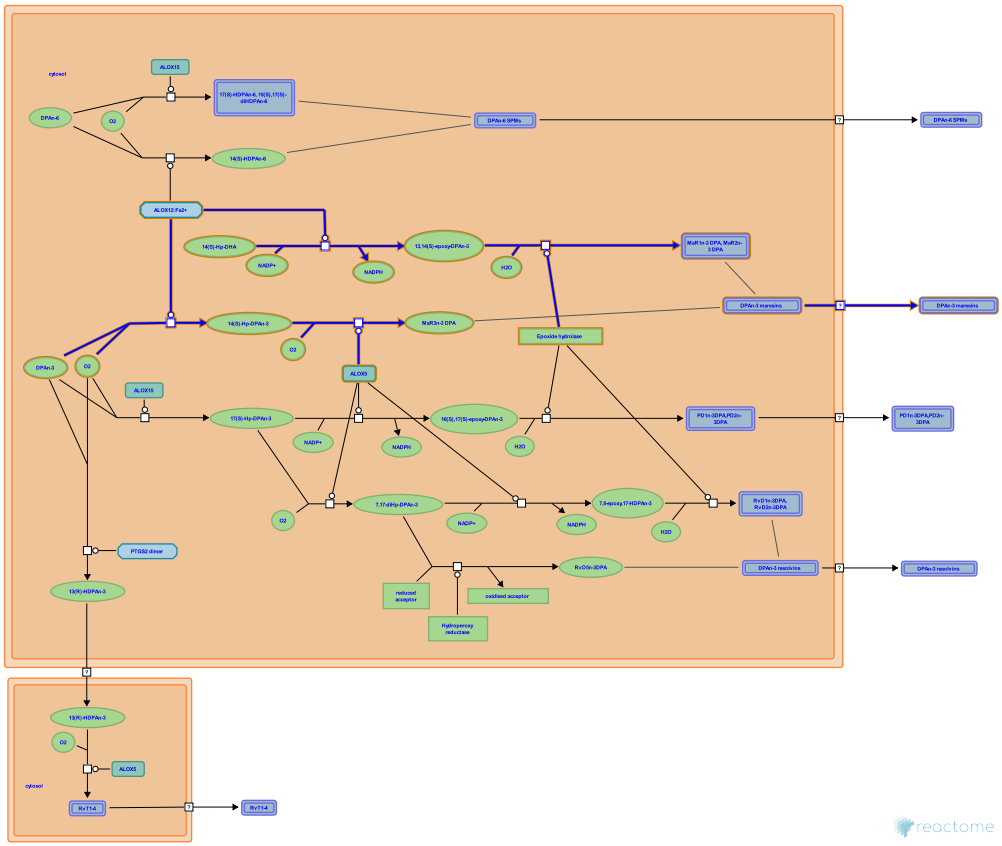
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Biosynthesis of DPAn-3-derived maresins ↗

Stable identifier: R-HSA-9026290



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).

Literature references

Serhan, CN., Colas, RA., Dalli, J. (2013). Novel n-3 immunoresolvents: structures and actions. *Sci Rep, 3*, 1940. ↗

Hansen, TV., Vik, A., Dalli, J. (2017). Recent advances in the chemistry and biology of anti-inflammatory and specialized pro-resolving mediators biosynthesized from n-3 docosapentaenoic acid. *Bioorg. Med. Chem. Lett., 27*, 2259-2266. ↗

Editions

2017-10-19	Authored, Edited	Jassal, B.
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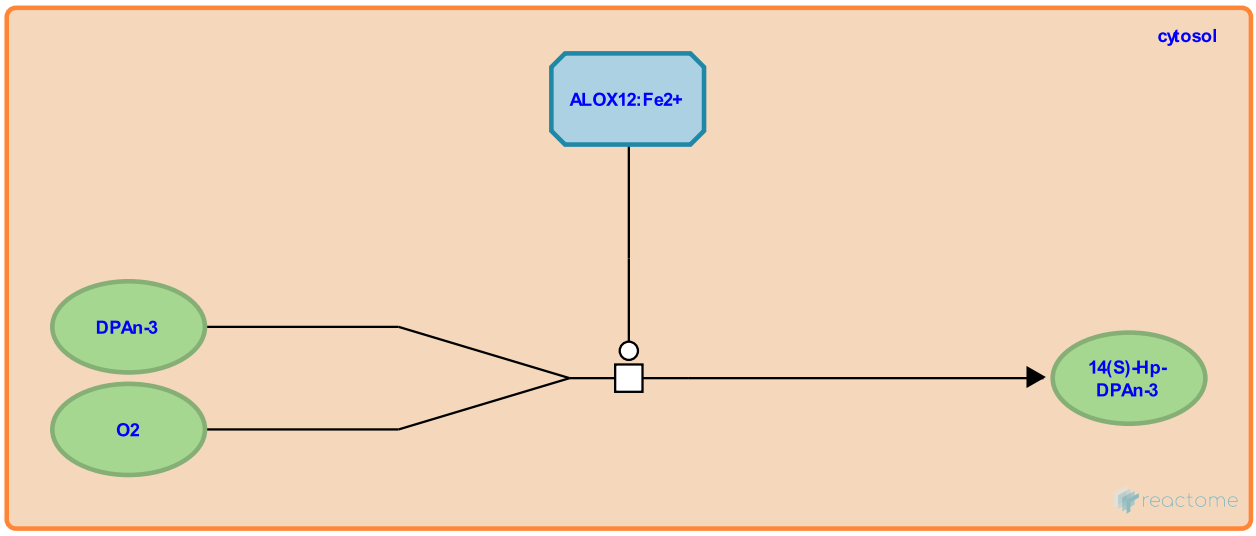
ALOX12:Fe2+ oxidises DPAn-3 to 14(S)-Hp-DPAn-3 ↗

Location: Biosynthesis of DPAn-3-derived maresins

Stable identifier: R-HSA-9026006

Type: transition

Compartments: cytosol



In a parallel pathway to 15-lipoxygenase-initiated protectin formation from ω-3 docosapentaenoic acid (DPAn-3), 12-lipoxygenase can also oxygenate DPAn-3 to form 14(S)-hydroperoxy-docosapentaenoic acid (14(S)-Hp-DPAn-3) (Dalli et al. 2013). This intermediate is the precursor for DPA-n-3-derived maresins.

Followed by: ALOX12:Fe2+ dehydrogenates 14(S)-Hp-DPAn-3 to 13,14-epoxy-DPAn-3

Literature references

Serhan, CN., Colas, RA., Dalli, J. (2013). Novel n-3 immunoresolvents: structures and actions. *Sci Rep, 3*, 1940. ↗

Editions

2017-10-16	Authored, Edited	Jassal, B.
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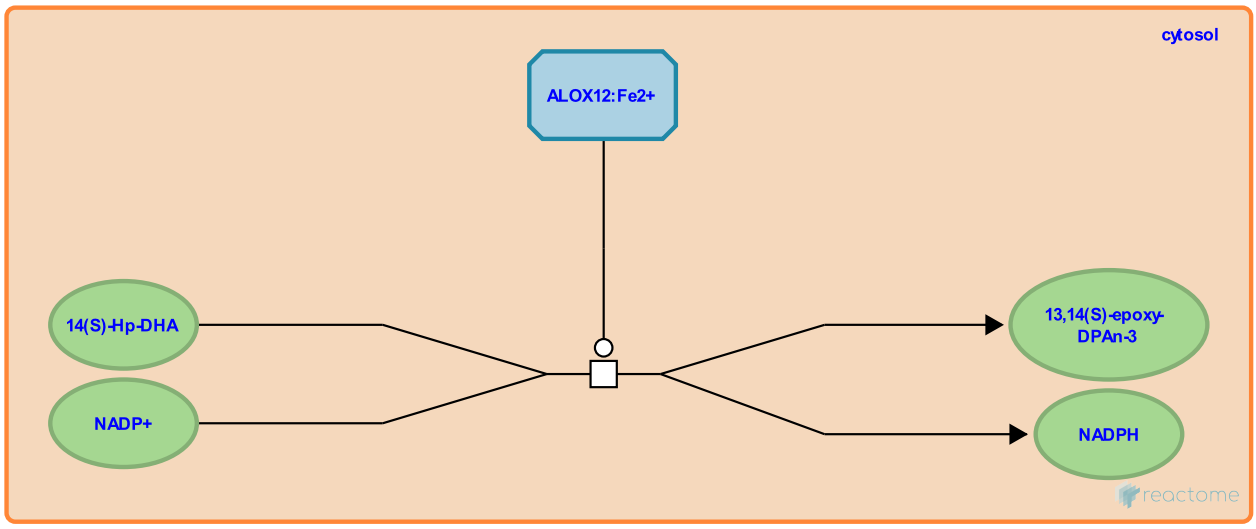
ALOX12:Fe2+ dehydrogenates 14(S)-Hp-DPAn-3 to 13,14-epoxy-DPAn-3 ↗

Location: Biosynthesis of DPAn-3-derived maresins

Stable identifier: R-HSA-9026007

Type: transition

Compartments: cytosol



In a reaction scheme that could be similar to the one for DHA-derived maresins, a lipoxygenase mediates the abstraction of hydrogen from 14(S)-hydroperoxy-docosapentaenoic acid (14(S)-Hp-DPAn-3) to form the epoxy product 13,14(S)-epoxy-docosapentaenoic acid (13,14(S)-epoxy-DPAn-3) (Dalli et al. 2013). If, as assumed, DPA metabolism follows the same path as for DHA metabolism, the lipoxygenase could be 12-lipoxygenase (ALOX12).

Preceded by: ALOX12:Fe2+ oxidises DPAn-3 to 14(S)-Hp-DPAn-3

Followed by: ALOX5 oxidises 14(S)-Hp-DPAn-3 to MaR3n-3 DPA, Epoxide hydrolase hydrolyses 13,14-epoxy-DPAn-3 to MaR1n-3 DPA or MaR2n-3 DPA

Literature references

Serhan, CN., Colas, RA., Dalli, J. (2013). Novel n-3 immunoresolvents: structures and actions. *Sci Rep, 3*, 1940. ↗

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2018-02-21	Reviewed	Hansen, TV.

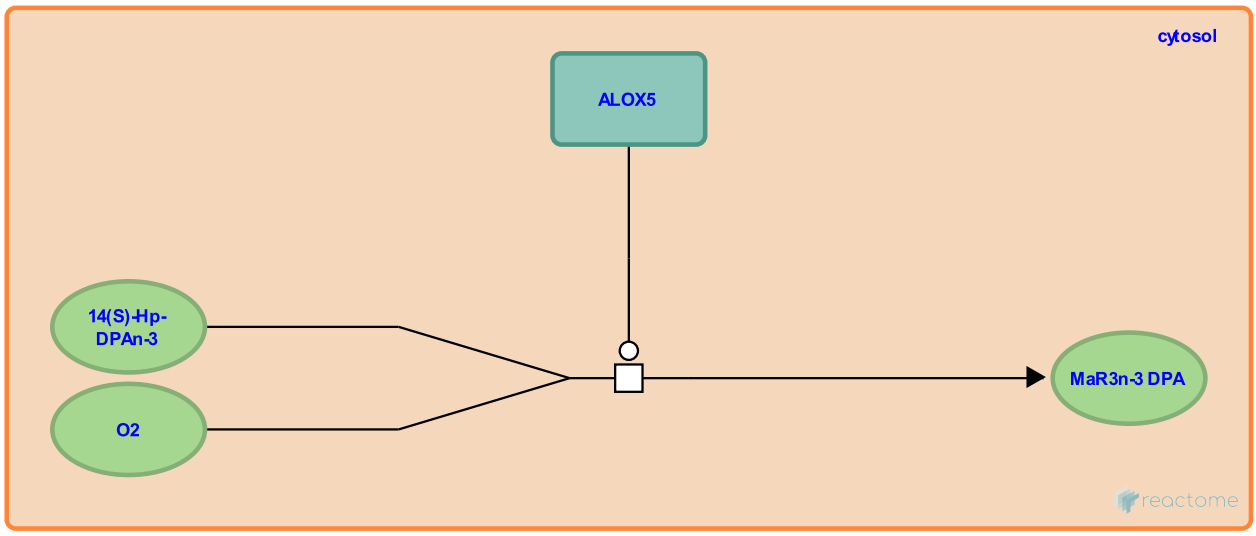
ALOX5 oxidises 14(S)-Hp-DPAn-3 to MaR3n-3 DPA ↗

Location: Biosynthesis of DPAn-3-derived maresins

Stable identifier: R-HSA-9026005

Type: transition

Compartments: cytosol



In an alternative reaction to epoxidation, 14(S)-hydroperoxy-docosapentaenoic acid (14(S)-HpDPAn-3) can undergo a second oxygenation at the ω-1 position to yield 14(S), 21-dihydroxy-docosapentaenoic acid (MaR3n-3 DPA) (Dalli et al. 2013). MaR3n-3 DPA is named after maresin-1 (derived from DHA) as they share an alcohol group at C14 and is proposed to possess similar anti-inflammatory and proresolving potency and activity as maresin-1. With human leukocytes this n-3 DPA-SPM reduced neutrophil chemotaxis, adhesion and enhanced macrophage phagocytosis (Dalli et al. 2013, Vik et al. 2017). If, as assumed, DPA metabolism follows the same path as DHA metabolism, the lipoxygenase could be the dual-functional 5-lipoxygenase (ALOX5).

Preceded by: ALOX12:Fe2+ dehydrogenates 14(S)-Hp-DPAn-3 to 13,14-epoxy-DPAn-3

Followed by: DPAn-3 maresins translocate from cytosol to extracellular region

Literature references

Serhan, CN., Colas, RA., Dalli, J. (2013). Novel n-3 immunoresolvents: structures and actions. *Sci Rep, 3*, 1940. ↗

Hansen, TV., Vik, A., Dalli, J. (2017). Recent advances in the chemistry and biology of anti-inflammatory and specialized pro-resolving mediators biosynthesized from n-3 docosapentaenoic acid. *Bioorg. Med. Chem. Lett., 27*, 2259-2266. ↗

Editions

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Epoxide hydrolase hydrolyses 13,14-epoxy-DPAn-3 to MaR1n-3 DPA or MaR2n-3 DPA

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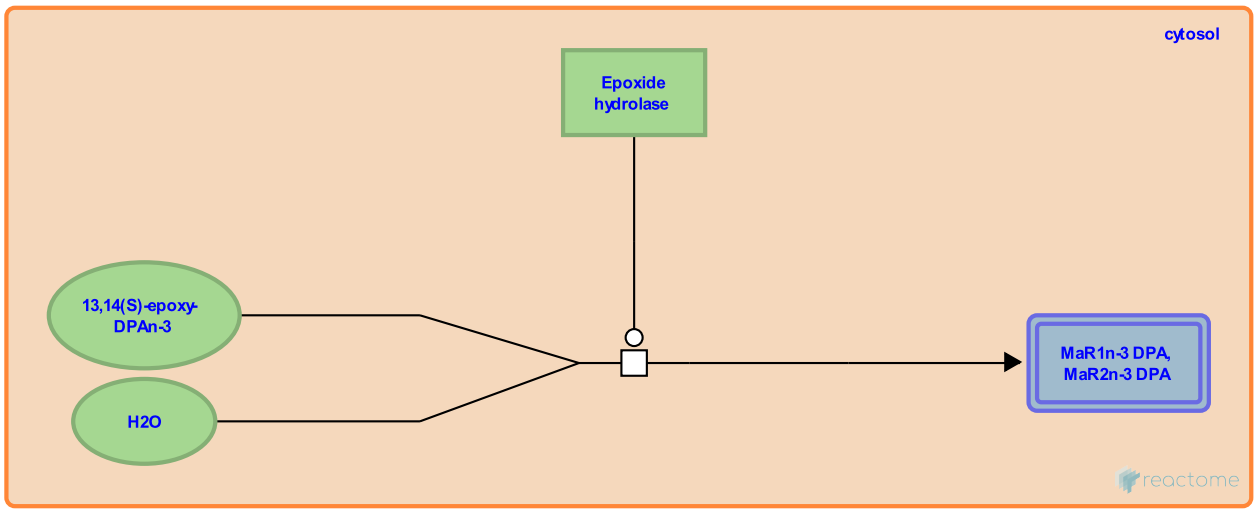
Location: Biosynthesis of DPAn-3-derived maresins

Stable identifier: R-HSA-9025998

Type: transition

Compartments: cytosol



In a reaction scheme similar to the one for DHA-derived maresins, 13,14(S)-epoxy-docosapentaenoic acid (13,14(S)-epoxy-DPAn-3) can be hydrolysed by an epoxide hydrolase to form either 7(R),14(S)-dihydroxy-docosapentaenoic acid (MaR1n-3 DPA) or 13,14(S)-dihydroxy-docosapentaenoic acid (MaR2n-3 DPA) (Dalli et al. 2013). MaR1n-3 DPA and MaR2n-3 DPA are named after maresin-1 (derived from DHA) as they share an alcohol group at C14 and are proposed to possess similar anti-inflammatory and proresolving potency and activity as maresin-1. With human leukocytes these n-3 DPA-SPMs reduced neutrophil chemotaxis, adhesion and enhanced macrophage phagocytosis (Dalli et al. 2013, Vik et al. 2017). The total chemical synthesis of MaR1n-3 DPA had been reported for the first time in 2014 (Tungen et al. 2014).

Preceded by: ALOX12:Fe2+ dehydrogenates 14(S)-Hp-DPAn-3 to 13,14-epoxy-DPAn-3

Followed by: DPAn-3 maresins translocate from cytosol to extracellular region

Literature references

Serhan, CN., Colas, RA., Dalli, J. (2013). Novel n-3 immunoresolvents: structures and actions. *Sci Rep, 3*, 1940. ↗

Serhan, CN., Hansen, TV., Tungen, JE., Aursnes, M., Arnardottir, H., Dalli, J. (2014). Total synthesis of the anti-inflammatory and pro-resolving lipid mediator MaR1n-3 DPA utilizing an sp(3) -sp(3) Negishi cross-coupling reaction. *Chemistry, 20*, 14575-8. ↗

Editions

2017-10-16	Authored, Edited	Jassal, B.
2018-02-21	Reviewed	Hansen, TV.

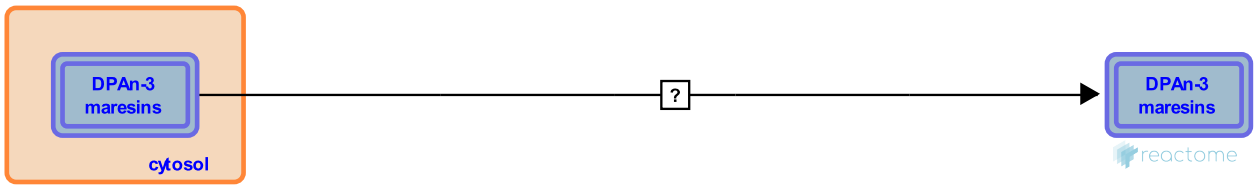
DPAn-3 maresins translocate from cytosol to extracellular region ↗

Location: Biosynthesis of DPAn-3-derived maresins

Stable identifier: R-HSA-9031894

Type: uncertain

Compartments: extracellular region, cytosol



To produce their pro-resolving effects, DPAn-3 derived maresins (MaR1n-3DPA, MaR2n-3DPA and MaR3n-3DPA) are released into the exudate of local inflammation sites (Dalli et al. 2013, Vik et al. 2017). The mechanism of translocation is unknown.

Preceded by: ALOX5 oxidises 14(S)-Hp-DPAn-3 to MaR3n-3 DPA, Epoxide hydrolase hydrolyses 13,14-epoxy-DPAn-3 to MaR1n-3 DPA or MaR2n-3 DPA

Literature references

Serhan, CN., Colas, RA., Dalli, J. (2013). Novel n-3 immunoresolvents: structures and actions. *Sci Rep, 3*, 1940. ↗

Hansen, TV., Vik, A., Dalli, J. (2017). Recent advances in the chemistry and biology of anti-inflammatory and specialized pro-resolving mediators biosynthesized from n-3 docosapentaenoic acid. *Bioorg. Med. Chem. Lett., 27*, 2259-2266. ↗

Editions

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