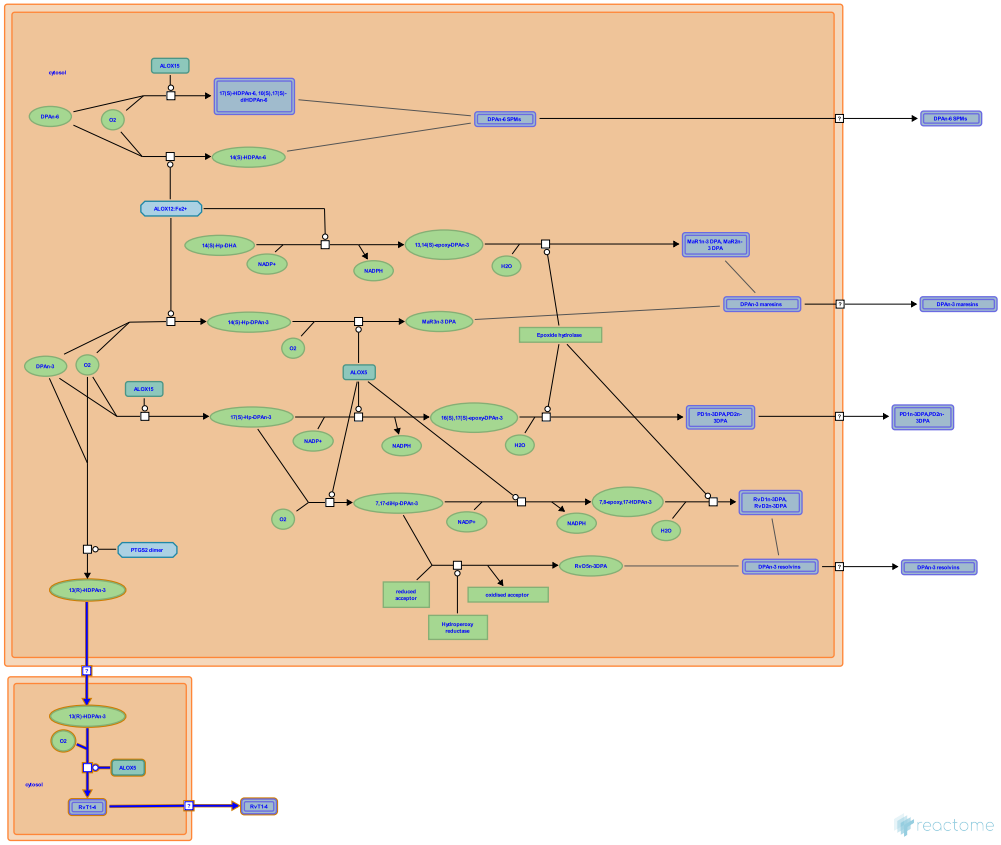
Biosynthesis of DPAn-3-derived 13-series resolvins



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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. ↗

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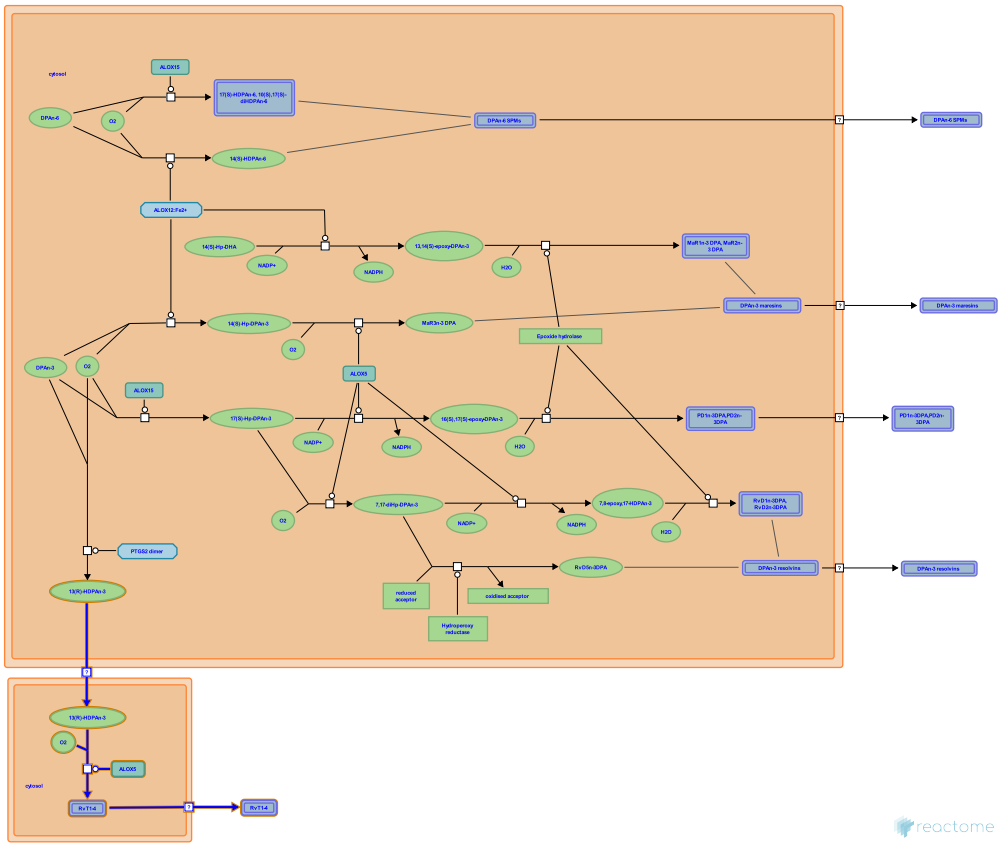
Biosynthesis of DPAn-3-derived 13-series resolvins ↗

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).

Literature references

Serhan, CN., Chiang, N., Dalli, J. (2015). Elucidation of novel 13-series resolvins that increase with atorvastatin and clear infections. *Nat. Med., 21*, 1071-5. ↗

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Serhan, CN., Colas, RA., Primdahl, KG., Hansen, TV., Aursnes, M., Walker, ME. et al. (2016). Synthesis of 13(R)-Hydroxy-7Z,10Z,13R,14E,16Z,19Z Docosapentaenoic Acid (13R-HDPA) and Its Biosynthetic Conversion to the 13-Series Resolvins. *J. Nat. Prod., 79*, 2693-2702. ↗

Editions

2017-10-19	Authored, Edited	Jassal, B.
2018-02-21	Reviewed	Hansen, TV.

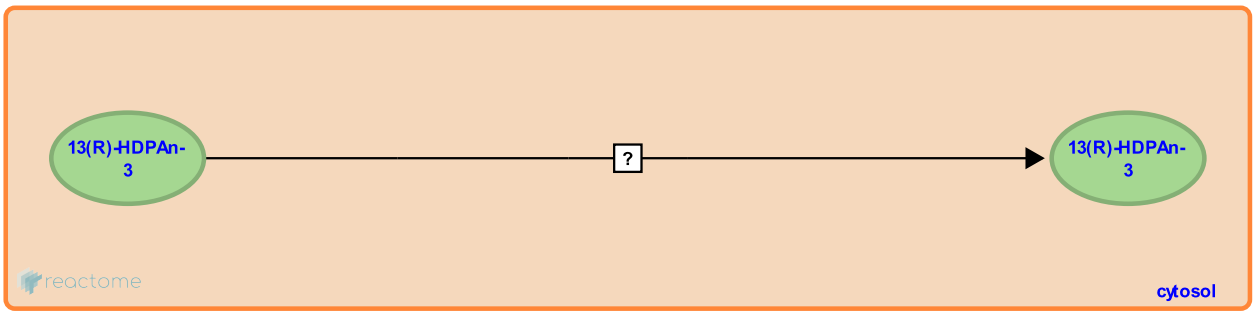
13(R)-HDPAn-3 translocates from endothelial cell to neutrophil ↗

Location: Biosynthesis of DPAn-3-derived 13-series resolvins

Stable identifier: R-HSA-9026411

Type: uncertain

Compartments: cytosol



13(R)-hydroxy-docosapentaenoic acid (13(R)-DPAn-3) translocates from endothelial cells to adhered neutrophils, where it can be oxidised further (Dalli et al. 2015, Primdahl et al. 2016).

Followed by: ALOX5 oxidises 13(R)-HDPAn-3 to RvT1-4

Literature references

Serhan, CN., Chiang, N., Dalli, J. (2015). Elucidation of novel 13-series resolvins that increase with atorvastatin and clear infections. *Nat. Med., 21*, 1071-5. ↗

Serhan, CN., Colas, RA., Primdahl, KG., Hansen, TV., Aursnes, M., Walker, ME. et al. (2016). Synthesis of 13(R)-Hydroxy-7Z,10Z,13R,14E,16Z,19Z Docosapentaenoic Acid (13R-HDPA) and Its Biosynthetic Conversion to the 13-Series Resolvins. *J. Nat. Prod., 79*, 2693-2702. ↗

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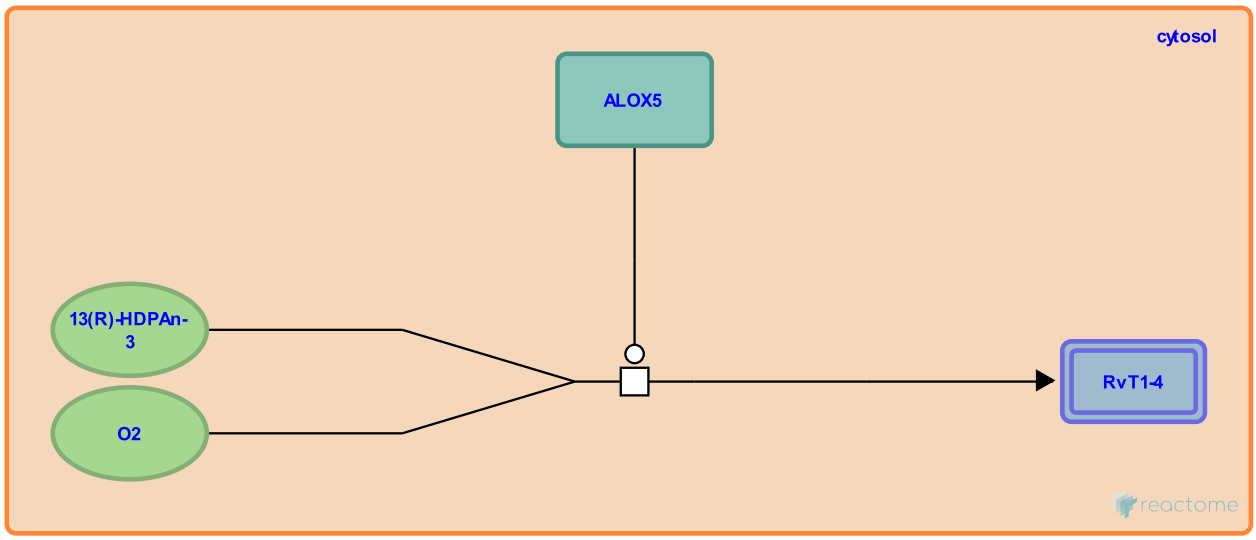
ALOX5 oxidises 13(R)-HDPAn-3 to RvT1-4 ↗

Location: Biosynthesis of DPAn-3-derived 13-series resolvins

Stable identifier: R-HSA-9026405

Type: transition

Compartments: cytosol



In neutrophils, 5-lipoxygenase (ALOX5) oxidises 13(R)-hydroxy-docosapentaenoic acid (13(R)-DPAn-3) to the 13(R)-resolvins RvT1-4 (7,13,20-trihydroxy-docosapentaenoic acid, 7,12,13-trihydroxy-docosapentaenoic acid, 7,8,13-trihydroxy-docosapentaenoic acid and 7,13-dihydroxy-docosapentaenoic acid respectively) (Dalli et al. 2015, Primdahl et al. 2016). They were all shown to posses anti-inflammatory and proresolving activities (Dalli et al. 2015). Recently, RvTs have been shown to mediate the proresolving actions of several statins in mice with inflammatory arthritis (Walker et al. 2017).

Preceded by: 13(R)-HDPAn-3 translocates from endothelial cell to neutrophil

Followed by: RvT1-4 translocate from cytosol to extracellular region

Literature references

Serhan, CN., Chiang, N., Dalli, J. (2015). Elucidation of novel 13-series resolvins that increase with atorvastatin and clear infections. *Nat. Med., 21*, 1071-5. ↗

Serhan, CN., Colas, RA., Primdahl, KG., Hansen, TV., Aursnes, M., Walker, ME. et al. (2016). Synthesis of 13(R)-Hydroxy-7Z,10Z,13R,14E,16Z,19Z Docosapentaenoic Acid (13R-HDPA) and Its Biosynthetic Conversion to the 13-Series Resolvins. *J. Nat. Prod., 79*, 2693-2702. ↗

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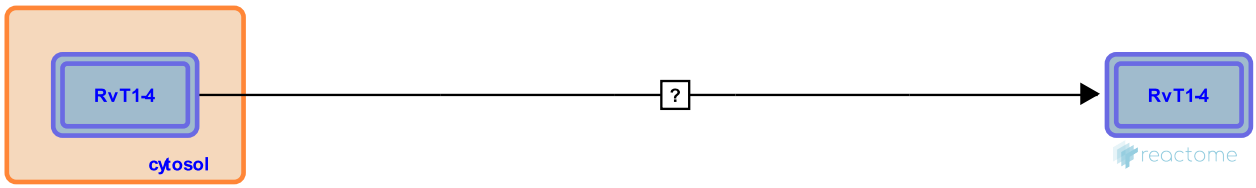
RvT1-4 translocate from cytosol to extracellular region ↗

Location: Biosynthesis of DPAn-3-derived 13-series resolvins

Stable identifier: R-HSA-9032021

Type: uncertain

Compartments: extracellular region, cytosol



To produce their pro-resolving effects, 13(R)-resolvins RvT1-4 are released into the exudate of local inflammation sites (Dalli et al. 2015, Walker et al. 2017). The mechanism of translocation is unknown.

Preceded by: ALOX5 oxidises 13(R)-HDPAn-3 to RvT1-4

Literature references

Serhan, CN., Chiang, N., Dalli, J. (2015). Elucidation of novel 13-series resolvins that increase with atorvastatin and clear infections. *Nat. Med., 21*, 1071-5. ↗

Colas, RA., Souza, PR., Walker, ME., Dalli, J. (2017). 13-Series resolvins mediate the leukocyte-platelet actions of atorvastatin and pravastatin in inflammatory arthritis. *FASEB J., 31*, 3636-3648. ↗

Editions

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2018-02-21	Reviewed	Hansen, TV.

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