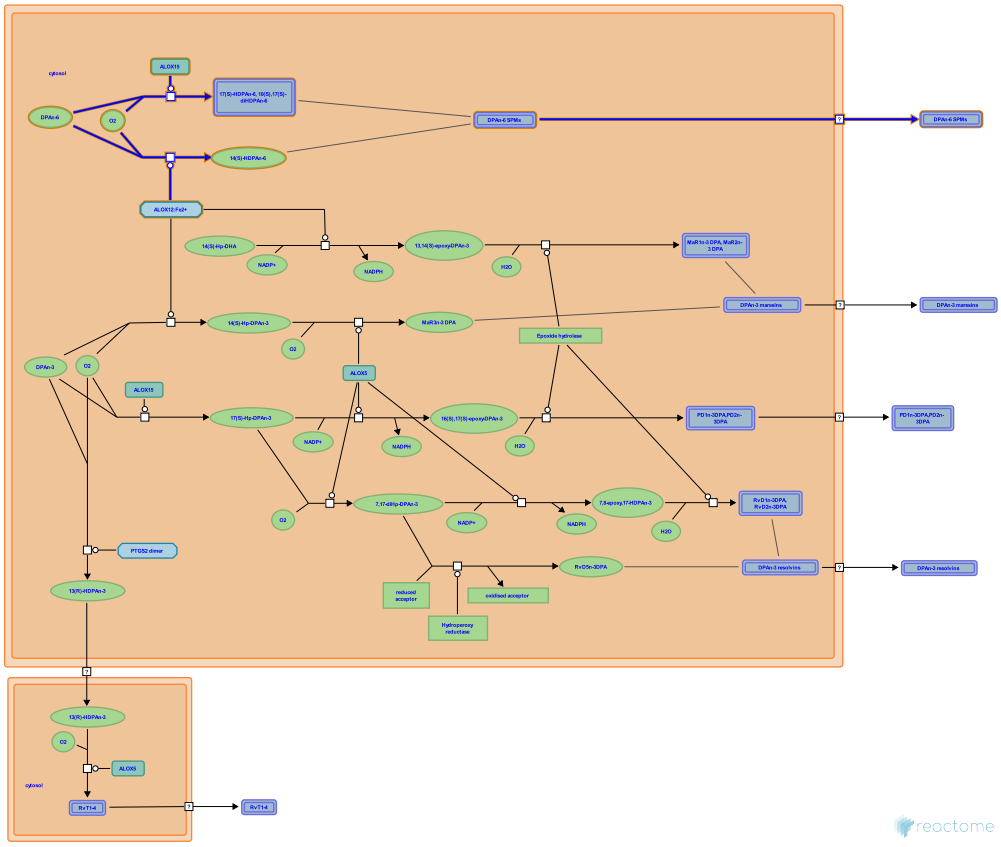
Biosynthesis of DPAn-6 SPMs



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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.

12/05/2024

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. ↗

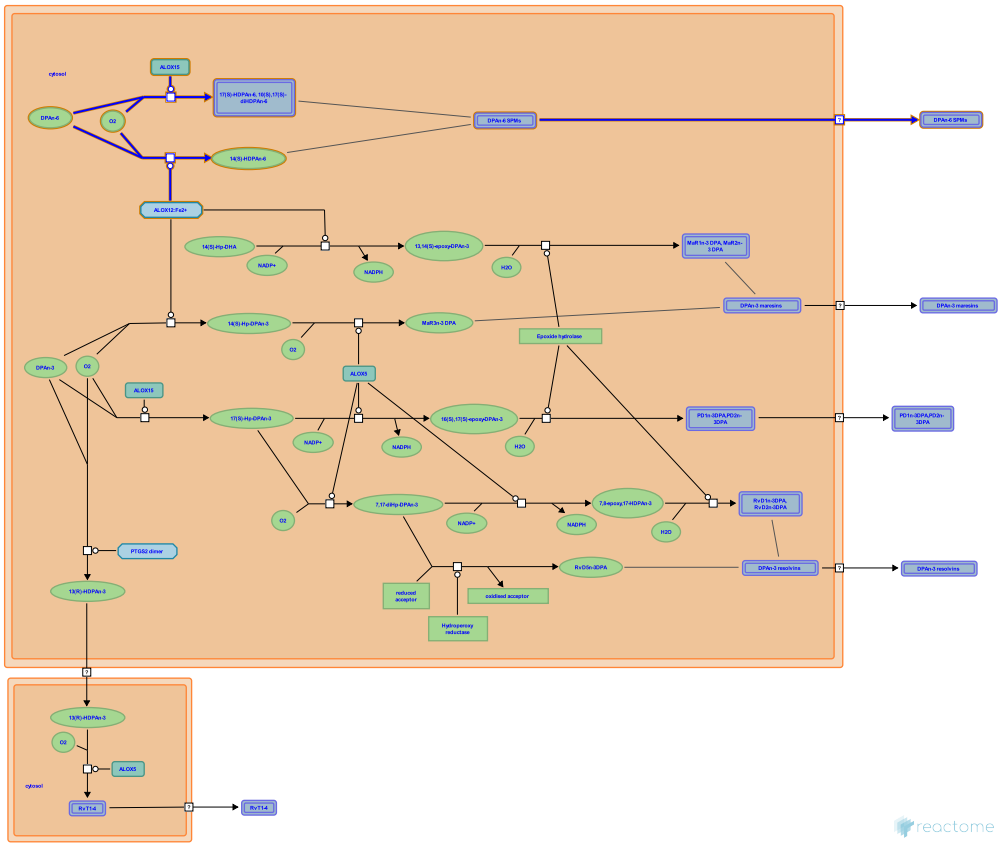
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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-6 SPMs ↗

Stable identifier: R-HSA-9025106



The biosynthesis of specialised proresolving mediators (SPMs) derived from the ω-6 isomer of DPA, DPAn-6 (cis-4,7,10,13,16-docosapentaenoic acid) is described here (Dangi et al. 2010). The products of the ω-6 isomer were characterised by analogy in structure and action to docosahexaenoic acid (DHA)-derived and eicosapentaenoic acid (EPA)-derived resolvins (Serhan et al. 2002, Bannenberg & Serhan 2010).

Literature references

Weylandt, KH. (2016). Docosapentaenoic acid derived metabolites and mediators - The new world of lipid mediator medicine in a nutshell. *Eur. J. Pharmacol., 785*, 108-115. ↗

Arterburn, LM., Hallenbeck, T., Chung, G., Nauroth, JM., Obeng, M., Dangi, B. et al. (2010). Metabolism and biological production of resolvins derived from docosapentaenoic acid (DPAn-6). *Biochem. Pharmacol., 79*, 251-60. ↗

Editions

2017-10-12	Authored, Edited	Jassal, B.
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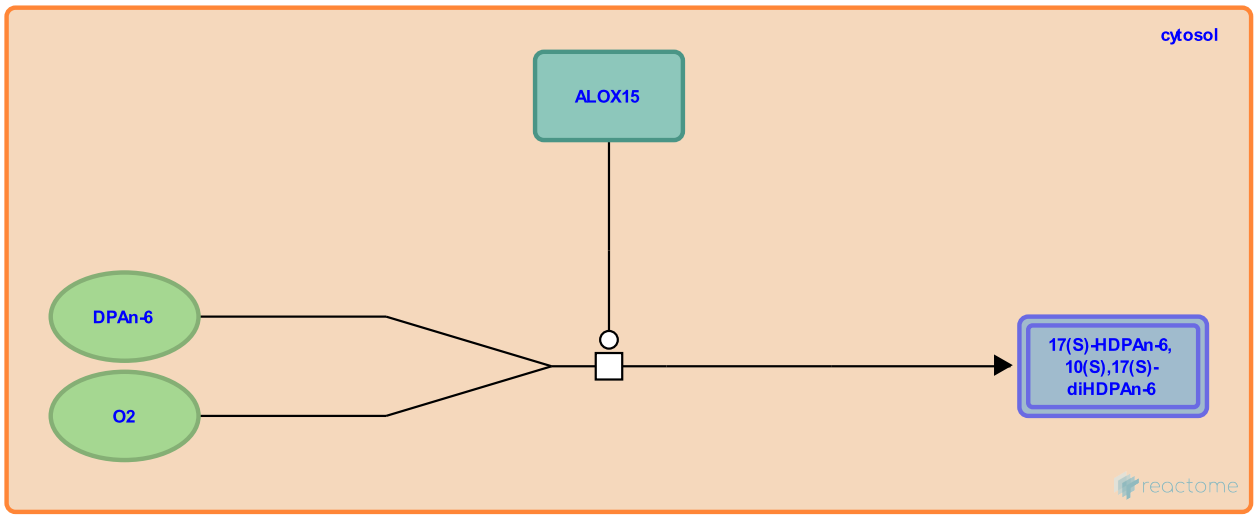
ALOX15 oxidises DPAn-6 to 17(S)-HDPAn-6 and 10(S),17(S)-diHDPAn-6

Location: Biosynthesis of DPAn-6 SPMs

Stable identifier: R-HSA-9025152

Type: transition

Compartments: cytosol



Of the 5-, 12- and 15-lipoxygenases, 15-lipoxygenase is the most efficient enzyme in oxygenating docosapentaenoic acids DPAn-6 and DPAn-3 as well as docosahexaenoic acid (DHA) at efficiencies 100%, 85% and 50% respectively. The main products of DPAn-6 oxygenation were found to be 17(S)-hydroxy-DPAn-6 and (10(S),17(S)-dihydroxy-DPAn-6 (17(S)-HDPAn-6 and 10(S),17(S)-diHDPAn-6 respectively) (Dangi et al. 2009, 2010, Dobson et al. 2013, Dayaker et al. 2014). Tested in two animal models of acute inflammation (Dangi et al. 2010) and human peripheral mononuclear cells (Nauroth et al. 2010), both compounds possessed potent anti-inflammatory activity. These DPAn-6 products are analogous in structure and action to DHA (docosahexaenoic acid)-derived resolvins (Dangi et al. 2010).

Followed by: DPAn-6 SPMs translocate from cytosol to extracellular region

Literature references

Durand, T., Balas, L., Dayaker, G. (2014). Total synthesis of neuroprotectin D1 analogues derived from omega-6 docosapentaenoic acid (DPA) and adrenic acid (AdA) from a common pivotal, late-stage intermediate. *J. Org. Chem., 79*, 2657-65.

Arterburn, LM., Liu, YC., Chung, G., Hall, EB., Nauroth, JM., Bell, R. et al. (2010). Docosahexaenoic acid (DHA) and docosapentaenoic acid (DPAn-6) algal oils reduce inflammatory mediators in human peripheral mononuclear cells in vitro and paw edema in vivo. *Lipids, 45*, 375-84.

Kralovec, JA., Dobson, EP., Adcock, JL., Barrow, CJ. (2013). Controlled formation of mono- and dihydroxy-resolvins from EPA and DHA using soybean 15-lipoxygenase. *J. Lipid Res., 54*, 1439-47.

Arterburn, LM., Hallenbeck, T., Chung, G., Nauroth, JM., Obeng, M., Dangi, B. et al. (2010). Metabolism and biological production of resolvins derived from docosapentaenoic acid (DPAn-6). *Biochem. Pharmacol., 79*, 251-60.

Needham, M., Arterburn, LM., Nauroth, JM., Teymourlouei, M., Obeng, M., Raman, K. et al. (2009). Biogenic synthesis, purification, and chemical characterization of anti-inflammatory resolvins derived from docosapentaenoic acid (DPAn-6). *J. Biol. Chem., 284*, 14744-59.

Editions

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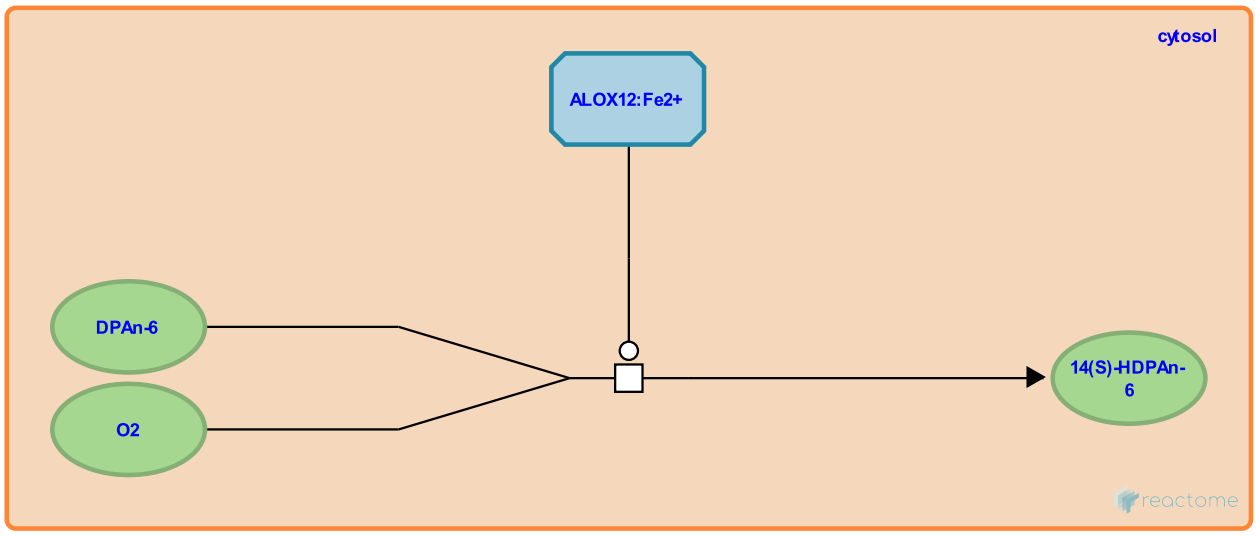
ALOX12:Fe2+ oxidises DPAn-6 to 14(S)-HDPAn-6 ↗

Location: Biosynthesis of DPAn-6 SPMs

Stable identifier: R-HSA-9025957

Type: transition

Compartments: cytosol



The main product of ω-6 docosapentaenoic acid (DPAn-6) oxygenation by 12-lipoxygenase (ALOX12:Fe2+) is 14(S)-hydroxy-DPAn-6 (14(S)-HDPAn-6) (Dangi et al. 2009, 2010, Dobson et al. 2013). The final product is produced via a hydroperoxy intermediate, which is then reduced to the corresponding hydroxy compound (these details not described here and also, the human enzymes involved in these reactions are unknown). This DPAn-6 product is analogous in structure and action to DHA (docosahexaenoic acid)-derived resolvins (Dangi et al. 2010).

Followed by: DPAn-6 SPMs translocate from cytosol to extracellular region

Literature references

Kralovec, JA., Dobson, EP., Adcock, JL., Barrow, CJ. (2013). Controlled formation of mono- and dihydroxy-resolvins from EPA and DHA using soybean 15-lipoxygenase. *J. Lipid Res., 54*, 1439-47. ↗

Arterburn, LM., Hallenbeck, T., Chung, G., Nauroth, JM., Obeng, M., Dangi, B. et al. (2010). Metabolism and biological production of resolvins derived from docosapentaenoic acid (DPAn-6). *Biochem. Pharmacol., 79*, 251-60. ↗

Needham, M., Arterburn, LM., Nauroth, JM., Teymourlouei, M., Obeng, M., Raman, K. et al. (2009). Biogenic synthesis, purification, and chemical characterization of anti-inflammatory resolvins derived from docosapentaenoic acid (DPAn-6). *J. Biol. Chem., 284*, 14744-59. ↗

Editions

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

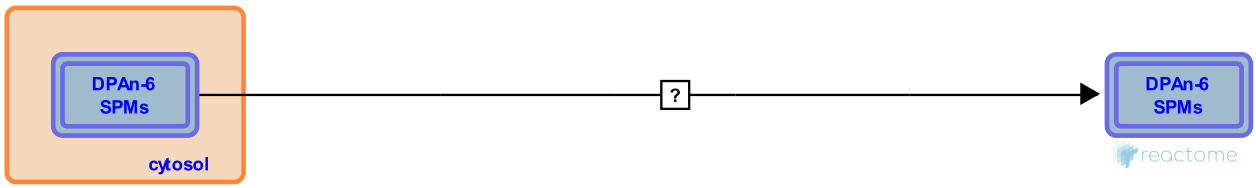
DPAn-6 SPMs translocate from cytosol to extracellular region ↗

Location: Biosynthesis of DPAn-6 SPMs

Stable identifier: R-HSA-9031884

Type: uncertain

Compartments: extracellular region, cytosol



To produce their pro-resolving effects, DPAn-6 SPMs are released into the exudate of local inflammation sites (Dangi et al. 2010). The mechanism of translocation is unknown.

Preceded by: ALOX12:Fe2+ oxidises DPAn-6 to 14(S)-HDPAn-6, ALOX15 oxidises DPAn-6 to 17(S)-HDPAn-6 and 10(S),17(S)-diHDPAn-6

Literature references

Arterburn, LM., Hallenbeck, T., Chung, G., Nauroth, JM., Obeng, M., Dangi, B. et al. (2010). Metabolism and biological production of resolvins derived from docosapentaenoic acid (DPAn-6). *Biochem. Pharmacol., 79*, 251-60. ↗

Editions

2017-12-04	Authored, Edited	Jassal, B.
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