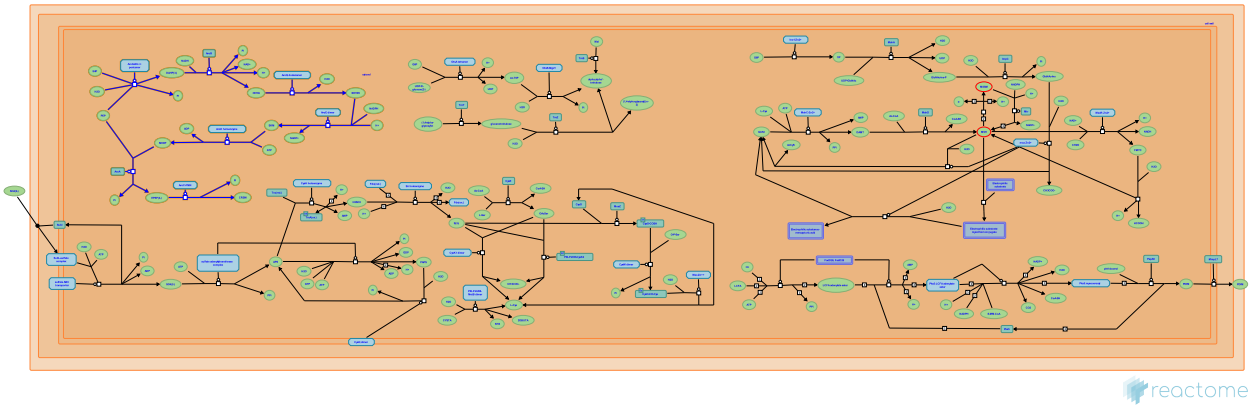
Chorismate via Shikimate Pathway



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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.

09/04/2024

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. ↗

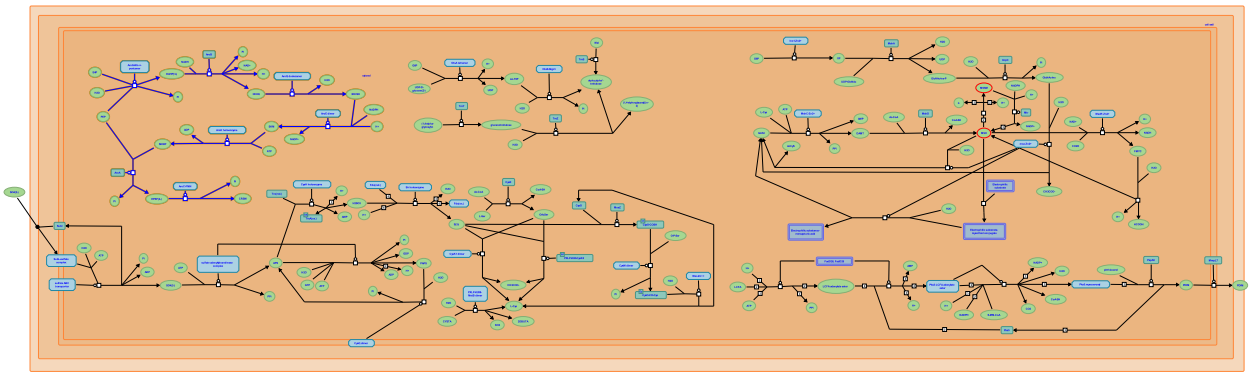
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Chorismate via Shikimate Pathway ↗

Stable identifier: R-MTU-964903

Compartments: cytosol



The shikimate pathway leads to the biosynthesis of chorismate, which, in mycobacteria, is a precursor of aromatic amino acids, naphthoquinones, menaquinones and siderophores. The enzymes of this pathway are attractive pharmaceutical targets, as the pathway is absent from mammals, and there are no redundancies in it (Herrmann and Weaver, 1999).

Literature references

Herrmann, KM., Weaver, LM. (1999). THE SHIKIMATE PATHWAY. *Annu Rev Plant Physiol Plant Mol Biol, 50*, 473-503. ↗

Editions

2010-09-13	Authored	Stephan, R.
2010-11-25	Reviewed	Warner, D.
2011-02-16	Edited	Jassal, B.

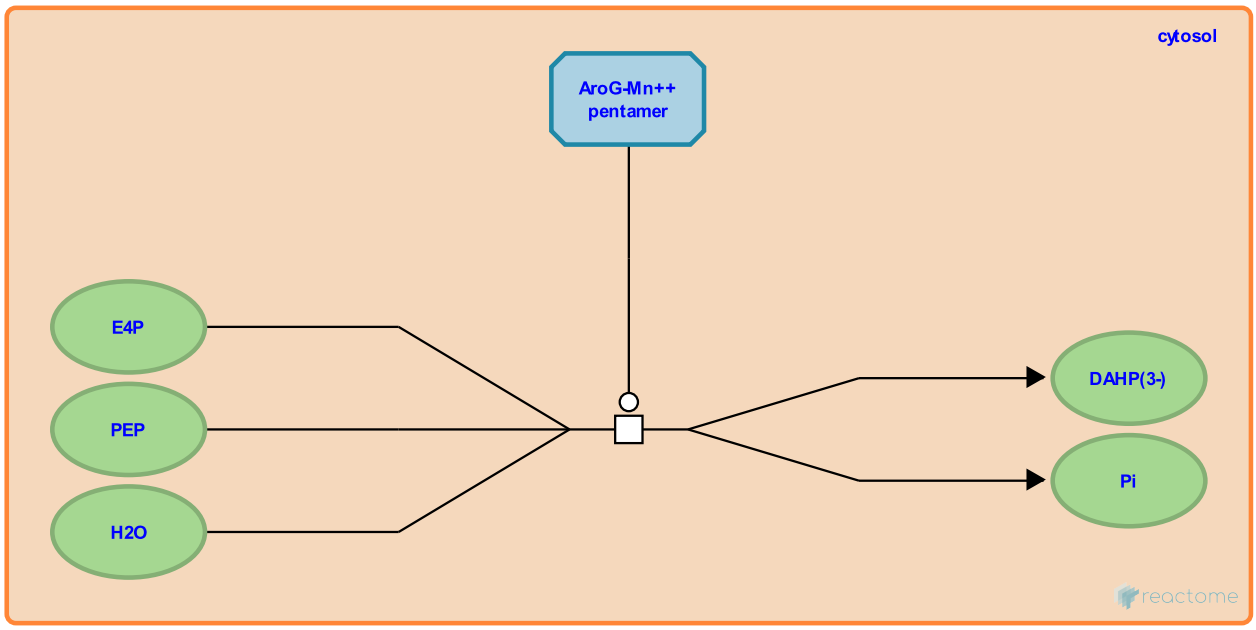
DHAP from Ery4P and PEP ↗

Location: Chorismate via Shikimate Pathway

Stable identifier: R-MTU-964912

Type: transition

Compartments: cytosol



The first committed step in the biosynthesis of chorismate is the fusion of D-erythrose-4-phosphate with phosphoenolpyruvate, catalyzed by AroG (Rizzi et al, 2005; Webby et al, 2005).

Followed by: DHQ from DAHP dephosphorylation

Literature references

Basso, LA., Oliveira, JS., da Fonseca, IO., Weber, PG., Santos, DS., Palma, MS. et al. (2005). DAHP synthase from Mycobacterium tuberculosis H37Rv: cloning, expression, and purification of functional enzyme. *Protein Expr Purif, 40*, 23-30. ↗

Baker, HM., Webby, CJ., Parker, EJ., Baker, EN., Lott, JS. (2005). The structure of 3-deoxy-d-arabino-heptulosonate 7-phosphate synthase from Mycobacterium tuberculosis reveals a common catalytic scaffold and ancestry for type I and type II enzymes. *J Mol Biol, 354*, 927-39. ↗

Editions

2010-09-13	Authored	Stephan, R.
2010-11-25	Reviewed	Warner, D.
2011-02-16	Edited	Jassal, B.

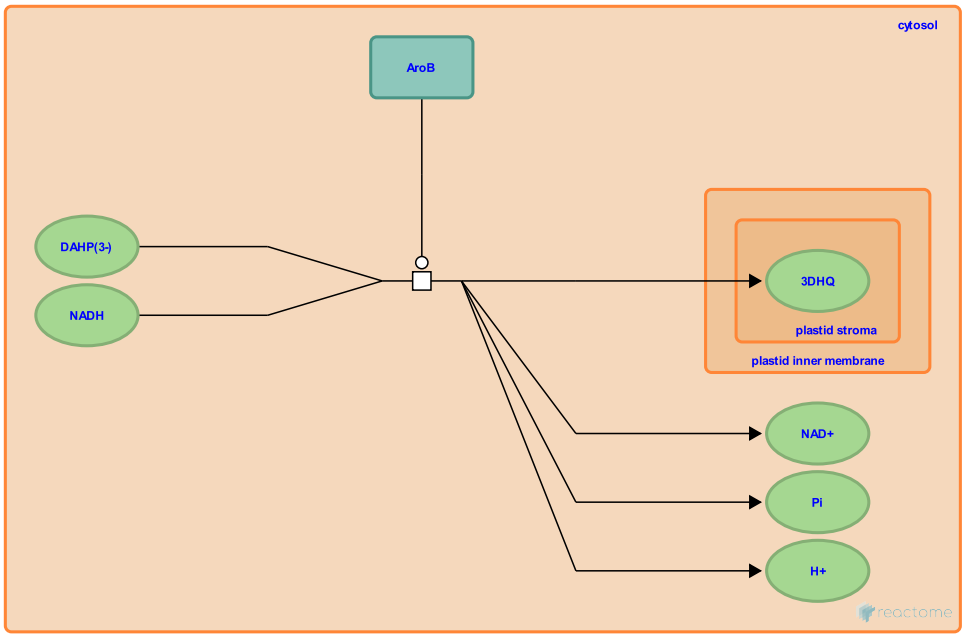
DHQ from DAHP dephosphorylation ↗

Location: Chorismate via Shikimate Pathway

Stable identifier: R-MTU-964914

Type: transition

Compartments: cytosol



Cyclization and dephosphorylation of DAHP, catalyzed by AroB, establishes the C6 ring in the pathway which is then only modified in the remaining five reactions (Mendonca et al, 2007).

Preceded by: DHAP from Ery4P and PEP

Followed by: Dehydratation of DHQ yields DHS

Literature references

Basso, LA., Santos, DS., de Mendonça, JD., Palma, MS., Frazzon, J., Ely, F. (2007). Functional characterization by genetic complementation of aroB-encoded dehydroquinate synthase from Mycobacterium tuberculosis H37Rv and its heterologous expression and purification. *J Bacteriol, 189*, 6246-52. ↗

Editions

2010-09-13	Authored	Stephan, R.
2010-11-25	Reviewed	Warner, D.
2011-02-16	Edited	Jassal, B.

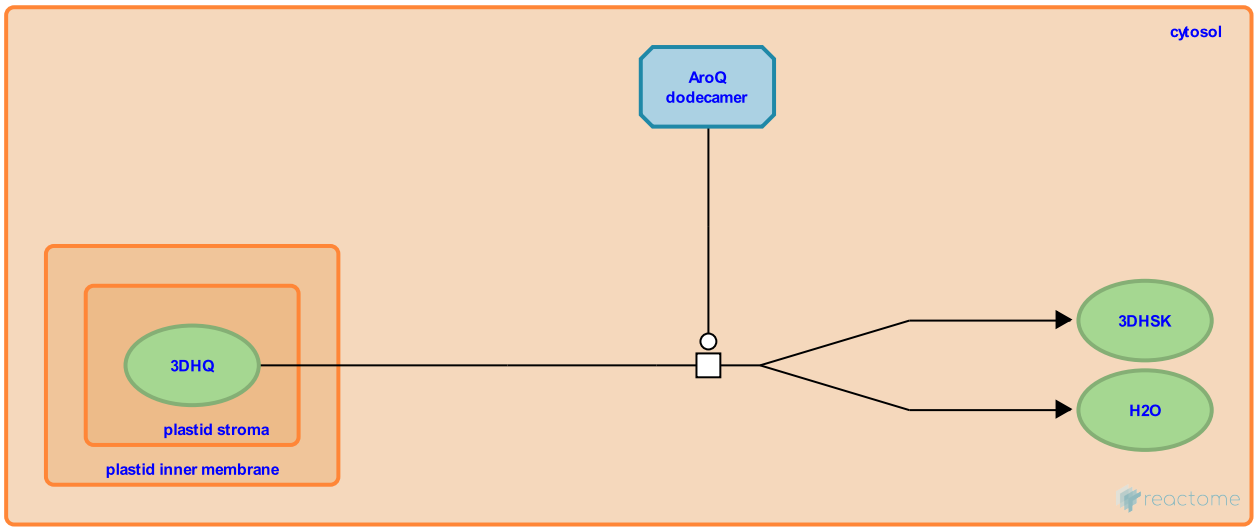
Dehydratation of DHQ yields DHS ↗

Location: Chorismate via Shikimate Pathway

Stable identifier: R-MTU-964851

Type: transition

Compartments: cytosol



AroQ, which catalyzes the dehydratation of 3-dehydroquinate (DHQ) to 3-dehydroshikimate (DHS), is a type II DHQ dehydratase. Unlike fungi DHQ dehydratases, AroQ doesn't take part in catabolism reactions (Moore et al, 1992).

Preceded by: DHQ from DAHP dephosphorylation

Followed by: Shikimate results from hydration of DHS

Literature references

Garbe, T., Lamb, HK., Hawkins, AR., Charles, IG., Moore, JD., Dougan, G. et al. (1992). Inducible overproduction of the Aspergillus nidulans pentafunctional AROM protein and the type-I and -II 3-dehydroquinases from Salmonella typhi and Mycobacterium tuberculosis. *Biochem J, 287,* 173-81. ↗

Editions

2010-09-13	Authored	Stephan, R.
2010-11-25	Reviewed	Warner, D.
2011-02-16	Edited	Jassal, B.

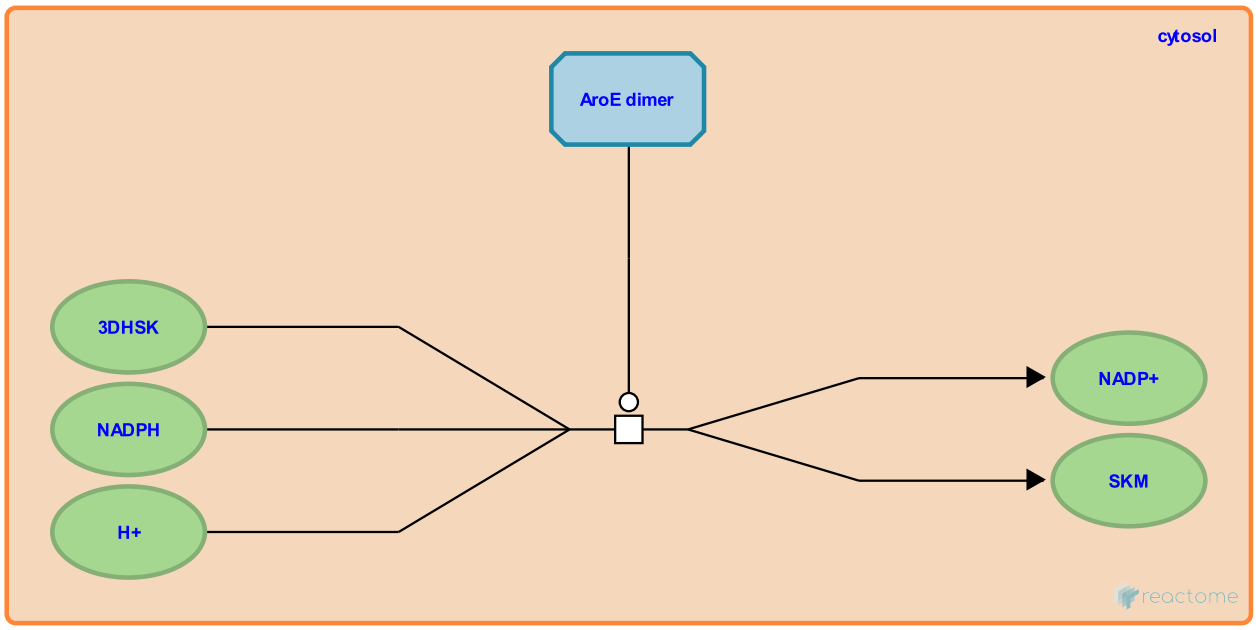
Shikimate results from hydration of DHS ↗

Location: Chorismate via Shikimate Pathway

Stable identifier: R-MTU-964842

Type: transition

Compartments: cytosol



The dimeric form of AroE catalyzes the hydration of dehydroshikimate. The reaction is reversible with high efficiency (Magalhaes et al, 2002; Fonseca et al, 2006).

Preceded by: Dehydratation of DHQ yields DHS

Followed by: Phosphorylation of shikimate

Literature references

Basso, LA., Oliveira, JS., Santos, DS., Palma, MS., Silva, RG., Magalhães, ML. et al. (2006). Functional shikimate dehydrogenase from Mycobacterium tuberculosis H37Rv: purification and characterization. *Protein Expr Purif, 46*, 429-37. ↗

Basso, LA., Santos, DS., Pereira, CP., Magalhães, ML. (2002). Cloning and expression of functional shikimate dehydrogenase (EC 1.1.1.25) from Mycobacterium tuberculosis H37Rv. *Protein Expr Purif, 26*, 59-64. ↗

Editions

2010-09-13	Authored	Stephan, R.
2010-11-25	Reviewed	Warner, D.
2011-02-16	Edited	Jassal, B.

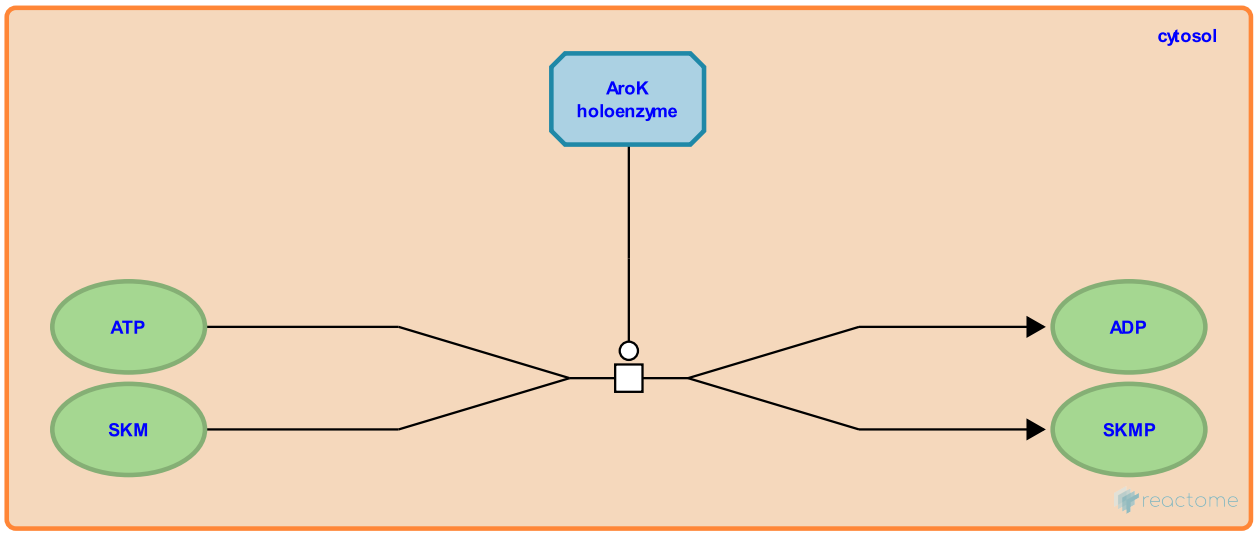
Phosphorylation of shikimate ↗

Location: Chorismate via Shikimate Pathway

Stable identifier: R-MTU-964939

Type: transition

Compartments: cytosol



Shikimate kinase (AroK) phosphorylates shikimate to shikimate 3-phosphate, using ATP (Oliveira et al, 2001).

Preceded by: Shikimate results from hydration of DHS

Followed by: EPSP from shikimate 3-phosphate

Literature references

Basso, LA., Oliveira, JS., Santos, DS., Pinto, CA. (2001). Cloning and overexpression in soluble form of functional shikimate kinase and 5-enolpyruvylshikimate 3-phosphate synthase enzymes from Mycobacterium tuberculosis. *Protein Expr Purif, 22*, 430-5. ↗

Editions

2010-09-13	Authored	Stephan, R.
2010-11-25	Reviewed	Warner, D.
2011-02-16	Edited	Jassal, B.

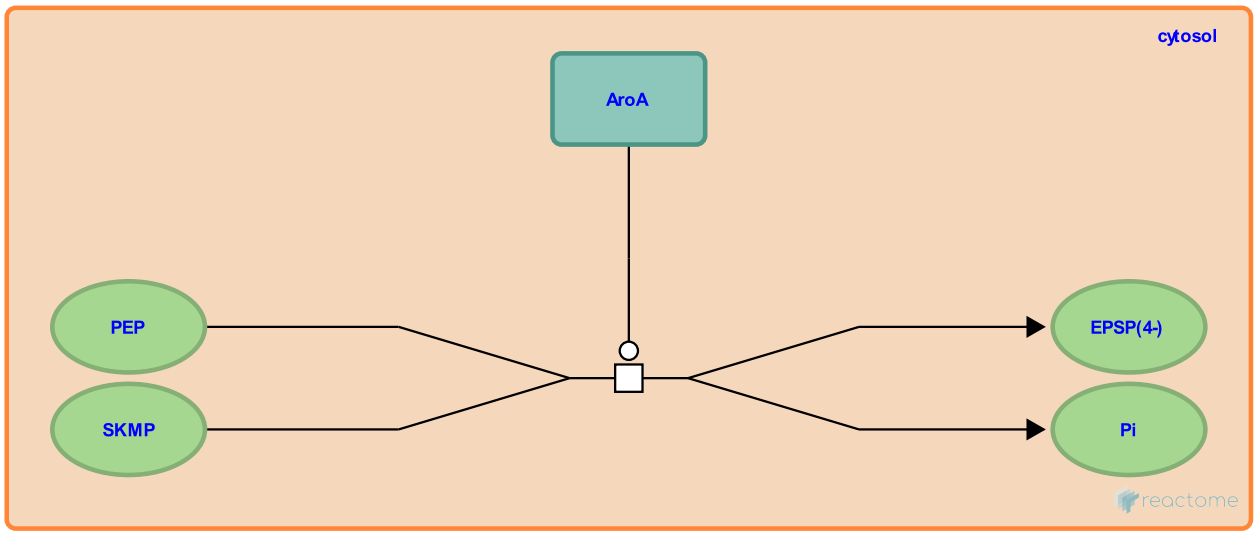
EPSP from shikimate 3-phosphate ↗

Location: Chorismate via Shikimate Pathway

Stable identifier: R-MTU-964886

Type: transition

Compartments: cytosol



Condensation with cleavage of one phosphate group of shikimate 3-phosphate and phosphoenolpyruvate to EPSP is catalyzed by AroA (Garbe et al, 1990).

Preceded by: Phosphorylation of shikimate

Followed by: Dephosphorylation of EPSP yields chorismate

Literature references

Jones, C., Garbe, T., Charles, I., Young, D., Dougan, G. (1990). Cloning and characterization of the aroA gene from Mycobacterium tuberculosis. *J Bacteriol, 172*, 6774-82. ↗

Editions

2010-09-13	Authored	Stephan, R.
2010-11-25	Reviewed	Warner, D.
2011-02-16	Edited	Jassal, B.

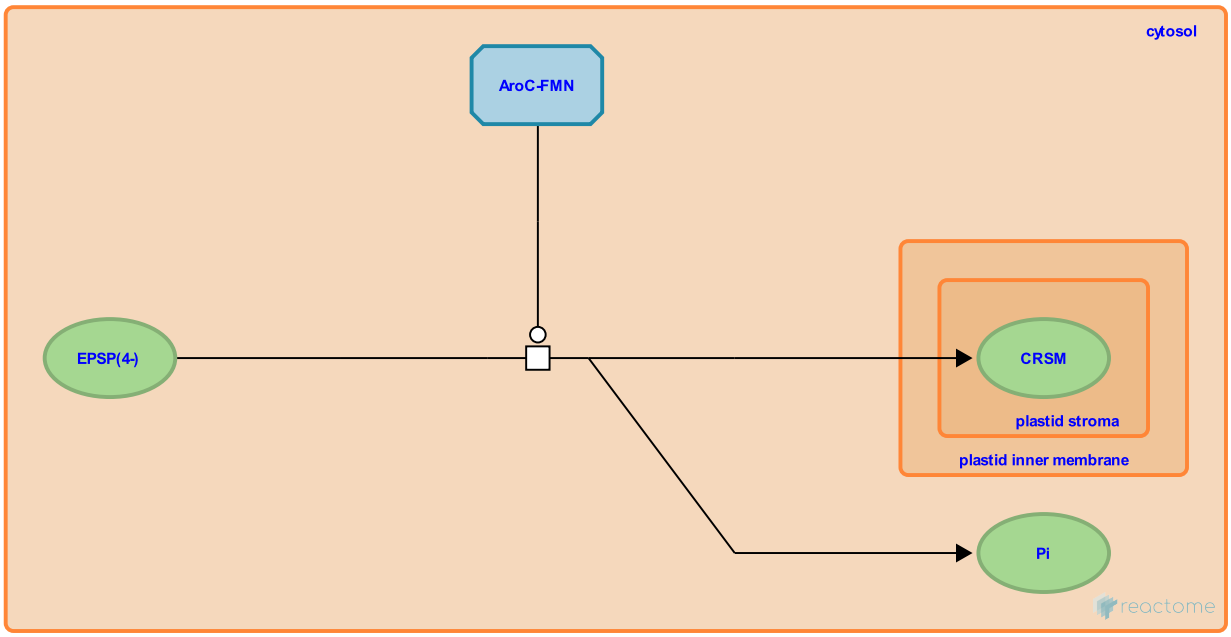
Dephosphorylation of EPSP yields chorismate ↗

Location: Chorismate via Shikimate Pathway

Stable identifier: R-MTU-964884

Type: transition

Compartments: cytosol



AroF in complex with reduced FMN catalyzes the dehydration and phosphate cleavage of EPSP, yielding chorismate. The cofactor FMN is reduced by NADPH which makes the enzyme stable in aerobic conditions and is known from similar fungal enzymes (Ely et al, 2008).

Preceded by: EPSP from shikimate 3-phosphate

Literature references

Basso, LA., Santos, DS., Palma, MS., Frazzon, J., Nunes, JE., Ely, F. et al. (2008). The Mycobacterium tuberculosis Rv2540c DNA sequence encodes a bifunctional chorismate synthase. *BMC Biochem, 9*, 13. ↗

Editions

2010-09-13	Authored	Stephan, R.
2010-11-25	Reviewed	Warner, D.
2011-02-16	Edited	Jassal, B.

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