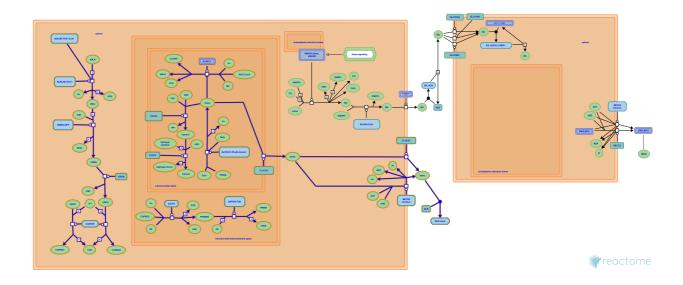


Heme biosynthesis



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

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of CC BY 4.0)
<u>License.</u> For more information see our License.

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.

18/05/2024

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 data-base: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968.

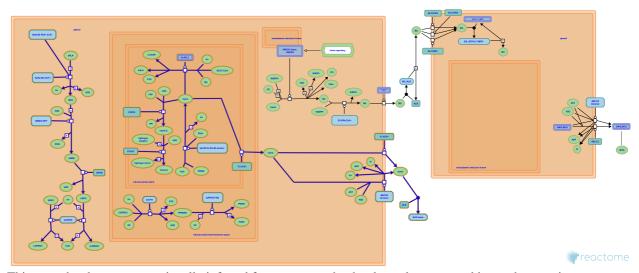
Reactome database release: 88

This document contains 1 pathway and 15 reactions (see Table of Contents)

Heme biosynthesis ↗

Stable identifier: R-CFA-189451

Inferred from: Heme biosynthesis (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

ALAS condenses SUCC-CoA and Gly to form dALA >

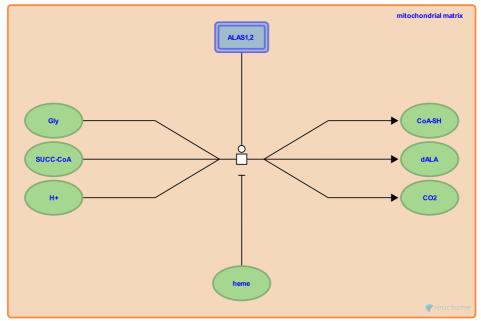
Location: Heme biosynthesis

Stable identifier: R-CFA-189442

Type: transition

Compartments: mitochondrial matrix

Inferred from: ALAS condenses SUCC-CoA and Gly to form dALA (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

ALAD condenses 2 dALAs to form PBG >

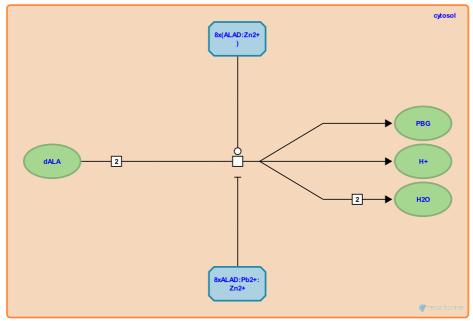
Location: Heme biosynthesis

Stable identifier: R-CFA-189439

Type: transition

Compartments: cytosol

Inferred from: ALAD condenses 2 dALAs to form PBG (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: 4 PBGs bind to form HMB

4 PBGs bind to form HMB **₹**

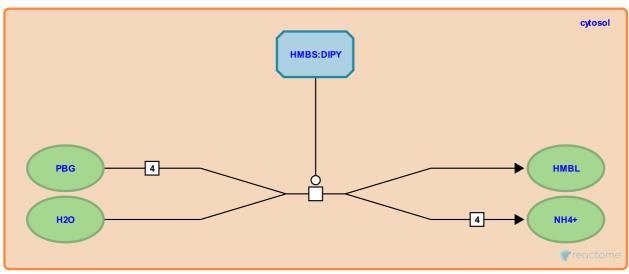
Location: Heme biosynthesis

Stable identifier: R-CFA-189406

Type: transition

Compartments: cytosol

Inferred from: 4 PBGs bind to form HMB (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: ALAD condenses 2 dALAs to form PBG

Followed by: UROS transforms HMB to URO3

UROS transforms HMB to URO3 对

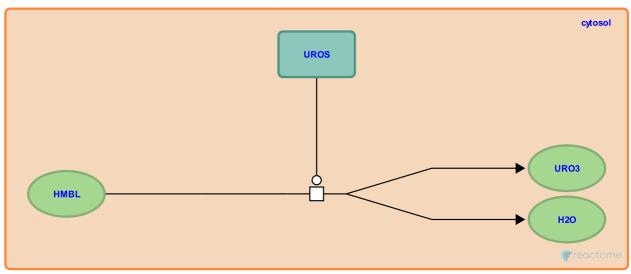
Location: Heme biosynthesis

Stable identifier: R-CFA-189488

Type: transition

Compartments: cytosol

Inferred from: UROS transforms HMB to URO3 (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: 4 PBGs bind to form HMB

Followed by: UROD decarboxylates URO3 to COPRO3

UROD decarboxylates URO3 to COPRO3 对

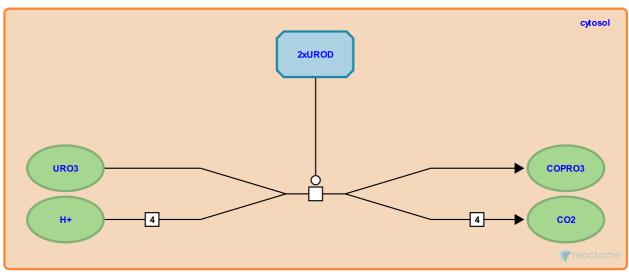
Location: Heme biosynthesis

Stable identifier: R-CFA-189425

Type: transition

Compartments: cytosol

Inferred from: UROD decarboxylates URO3 to COPRO3 (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: UROS transforms HMB to URO3

UROD decarboxylates URO1 to COPRO1 对

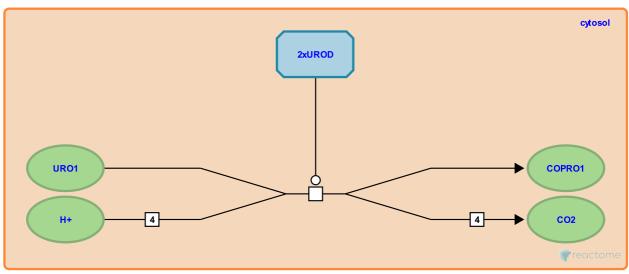
Location: Heme biosynthesis

Stable identifier: R-CFA-190182

Type: transition

Compartments: cytosol

Inferred from: UROD decarboxylates URO1 to COPRO1 (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

CPO transforms COPRO3 to PPGEN9

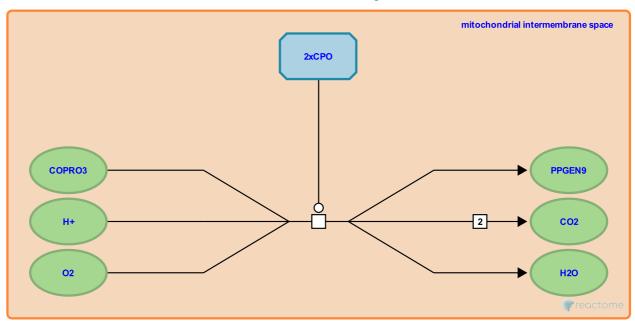
Location: Heme biosynthesis

Stable identifier: R-CFA-189421

Type: transition

Compartments: mitochondrial intermembrane space

Inferred from: CPO transforms COPRO3 to PPGEN9 (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: PPO oxidises PPGEN9 to PRIN9

PPO oxidises PPGEN9 to PRIN9 **↗**

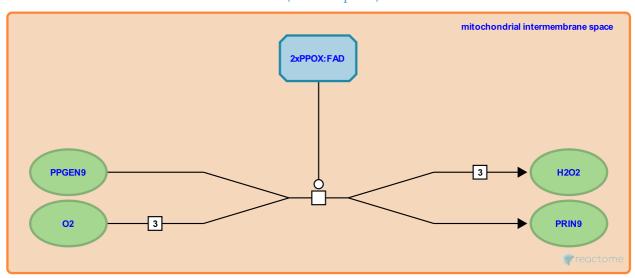
Location: Heme biosynthesis

Stable identifier: R-CFA-189423

Type: transition

Compartments: mitochondrial intermembrane space

Inferred from: PPO oxidises PPGEN9 to PRIN9 (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: CPO transforms COPRO3 to PPGEN9

FECH binds Fe2+ to PRIN9 to form heme **→**

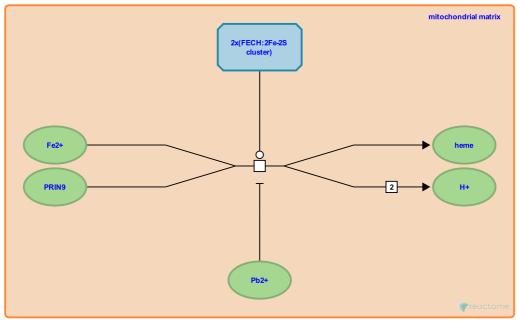
Location: Heme biosynthesis

Stable identifier: R-CFA-189465

Type: transition

Compartments: mitochondrial matrix

Inferred from: FECH binds Fe2+ to PRIN9 to form heme (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Followed by: COX10 transforms heme to heme O

FLVCR1-2 transports heme from mitochondrial matrix to cytosol 7

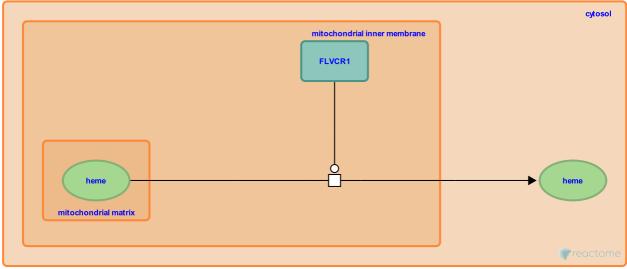
Location: Heme biosynthesis

Stable identifier: R-CFA-9661408

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix, cytosol

Inferred from: FLVCR1-2 transports heme from mitochondrial matrix to cytosol (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

ABCG2 tetramer transports heme from cytosol to extracellular region 7

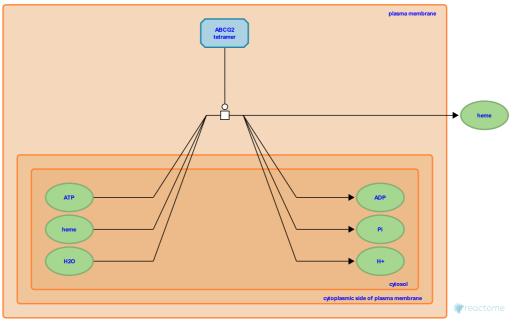
Location: Heme biosynthesis

Stable identifier: R-CFA-917979

Type: transition

Compartments: plasma membrane

Inferred from: ABCG2 tetramer transports heme from cytosol to extracellular region (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

FLVCR1-1 transports heme from cytosol to extracellular region 7

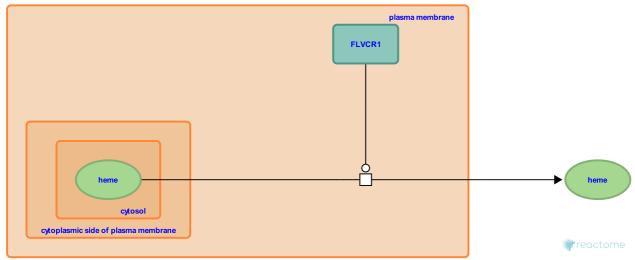
Location: Heme biosynthesis

Stable identifier: R-CFA-917892

Type: transition

Compartments: plasma membrane

Inferred from: FLVCR1-1 transports heme from cytosol to extracellular region (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

ALB binds extracellular heme 7

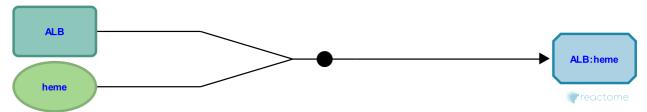
Location: Heme biosynthesis

Stable identifier: R-CFA-9661419

Type: binding

Compartments: extracellular region

Inferred from: ALB binds extracellular heme (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

COX10 transforms heme to heme 0 7

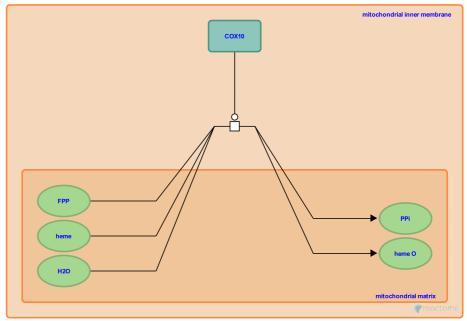
Location: Heme biosynthesis

Stable identifier: R-CFA-2995330

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix

Inferred from: COX10 transforms heme to heme O (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: FECH binds Fe2+ to PRIN9 to form heme

Followed by: COX15 transforms heme O to heme A

COX15 transforms heme O to heme A **7**

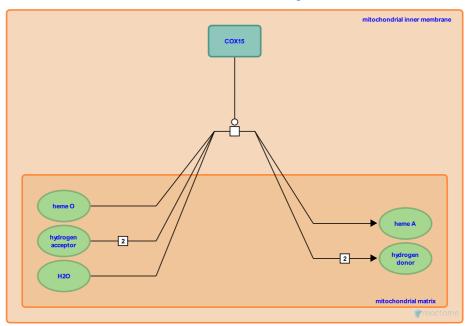
Location: Heme biosynthesis

Stable identifier: R-CFA-2995334

Type: transition

Compartments: mitochondrial inner membrane, mitochondrial matrix

Inferred from: COX15 transforms heme O to heme A (Homo sapiens)



This event has been computationally inferred from an event that has been demonstrated in another species.

The inference is based on the homology mapping from PANTHER. Briefly, reactions for which all involved PhysicalEntities (in input, output and catalyst) have a mapped orthologue/paralogue (for complexes at least 75% of components must have a mapping) are inferred to the other species. High level events are also inferred for these events to allow for easier navigation.

More details and caveats of the event inference in Reactome. For details on PANTHER see also: http://www.pantherdb.org/about.jsp

Preceded by: COX10 transforms heme to heme O

Table of Contents

ntro	duction	1
¥Η	eme biosynthesis	2
﴾	ALAS condenses SUCC-CoA and Gly to form dALA	3
﴾	ALAD condenses 2 dALAs to form PBG	4
﴾	4 PBGs bind to form HMB	5
﴾	UROS transforms HMB to URO3	6
﴾	UROD decarboxylates URO3 to COPRO3	7
﴾	UROD decarboxylates URO1 to COPRO1	8
﴾	CPO transforms COPRO3 to PPGEN9	9
﴾	PPO oxidises PPGEN9 to PRIN9	10
﴾	FECH binds Fe2+ to PRIN9 to form heme	11
﴾	FLVCR1-2 transports heme from mitochondrial matrix to cytosol	12
﴾	ABCG2 tetramer transports heme from cytosol to extracellular region	13
﴾	FLVCR1-1 transports heme from cytosol to extracellular region	14
→	ALB binds extracellular heme	15
→	COX10 transforms heme to heme O	16
→	COX15 transforms heme O to heme A	17
ГаЫ]	e of Contents	12