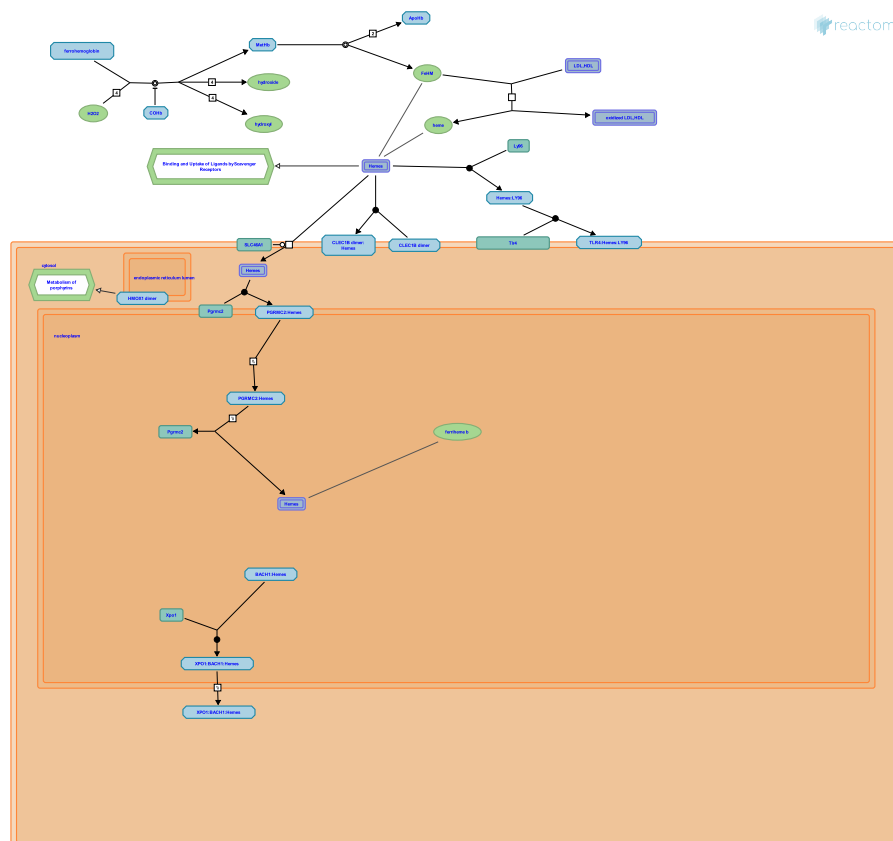


Heme signaling



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

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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](https://reactome.org/textbook/).

05/05/2024

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. [↗](#)

Reactome database release: 88

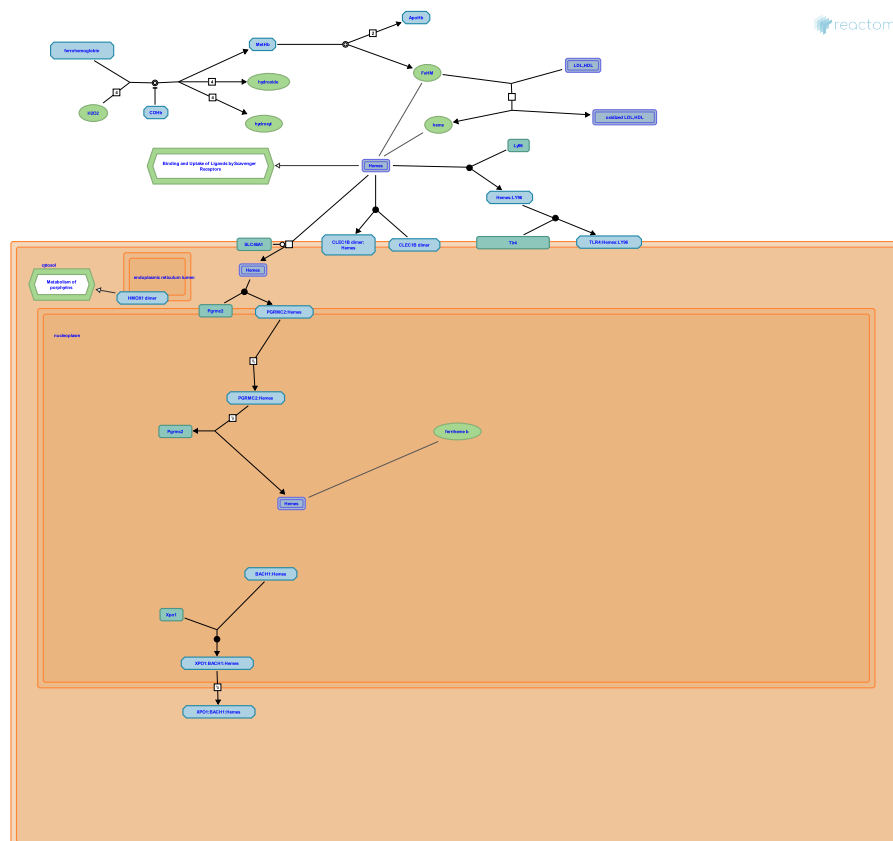
This document contains 1 pathway and 12 reactions ([see Table of Contents](#))

Heme signaling ↗

Stable identifier: R-RNO-9707616

Compartments: cytosol, extracellular region, nuclear envelope, nucleoplasm, plasma membrane

Inferred from: [Heme signaling \(Homo sapiens\)](#)



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>

H2O2 oxidises ferrohemoglobin to MetHb ↗

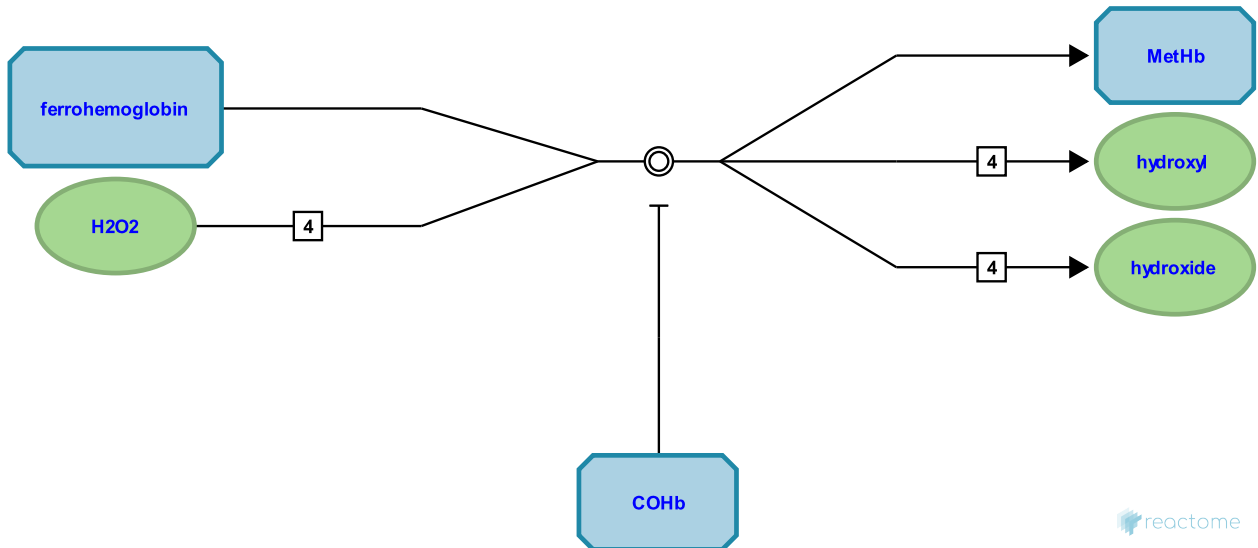
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707504

Type: dissociation

Compartments: extracellular region

Inferred from: [H2O2 oxidises ferrohemoglobin to MetHb \(Homo sapiens\)](#)



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: [FeHM dissociates from MetHb](#)

FeHM dissociates from MetHb ↗

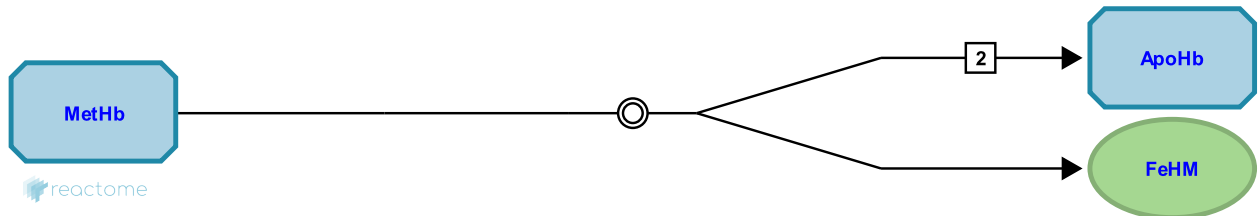
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707516

Type: dissociation

Compartments: extracellular region

Inferred from: [FeHM dissociates from MetHb \(Homo sapiens\)](#)



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: [H2O2 oxidises ferrohemoglobin to MetHb](#)

Followed by: [FeHM oxidises LDL,HDL](#)

FeHM oxidises LDL,HDL ↗

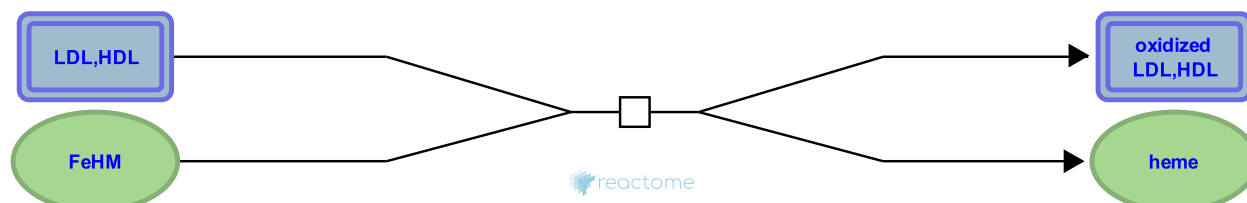
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707586

Type: transition

Compartments: extracellular region

Inferred from: [FeHM oxidises LDL,HDL \(Homo sapiens\)](#)



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: [FeHM dissociates from MetHb](#)

Hemes bind LY96 ↗

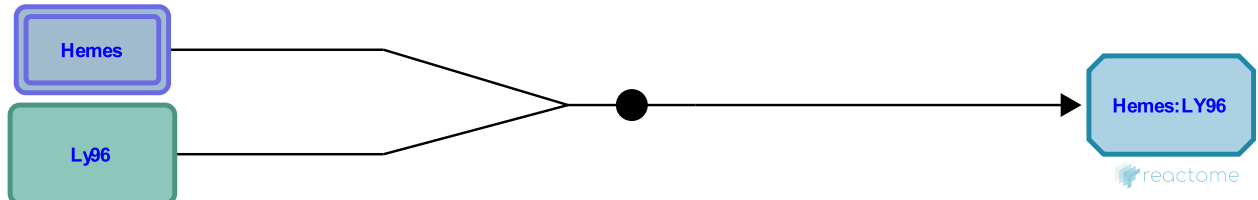
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707594

Type: binding

Compartments: extracellular region

Inferred from: [Hemes bind LY96 \(Homo sapiens\)](#)



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: [Hemes:LY96 activates TLR4](#)

Hemes:LY96 activates TLR4 [↗](#)

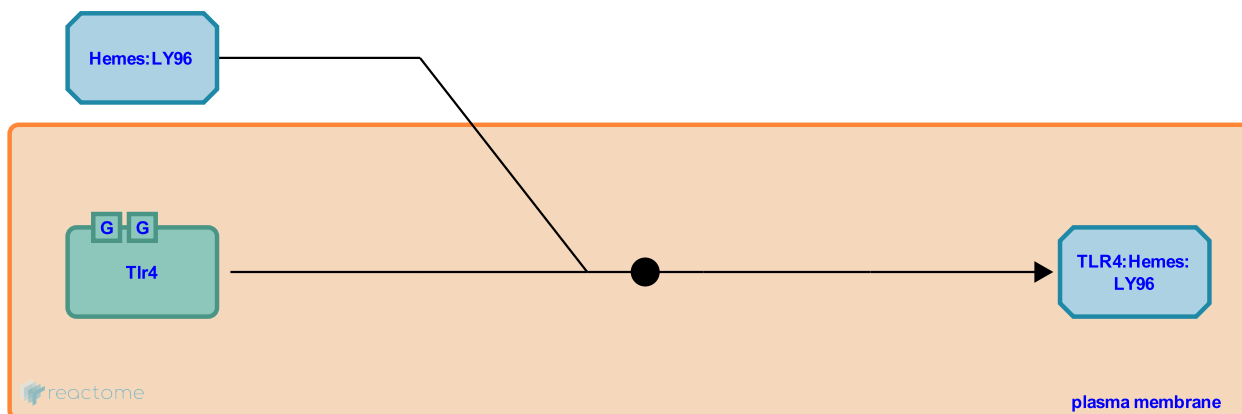
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707659

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: [Hemes:LY96 activates TLR4 \(Homo sapiens\)](#)



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: [Hemes bind LY96](#)

Hemes bind to CLEC1B dimer ↗

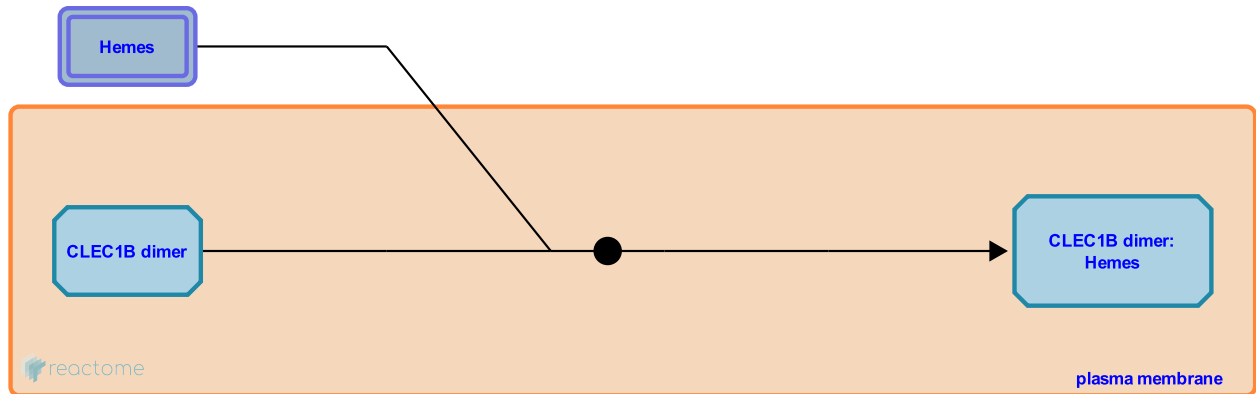
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707505

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: [Hemes bind to CLEC1B dimer \(Homo sapiens\)](#)



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>

SLC46A1 transports hemes from extracellular region to cytosol ↗

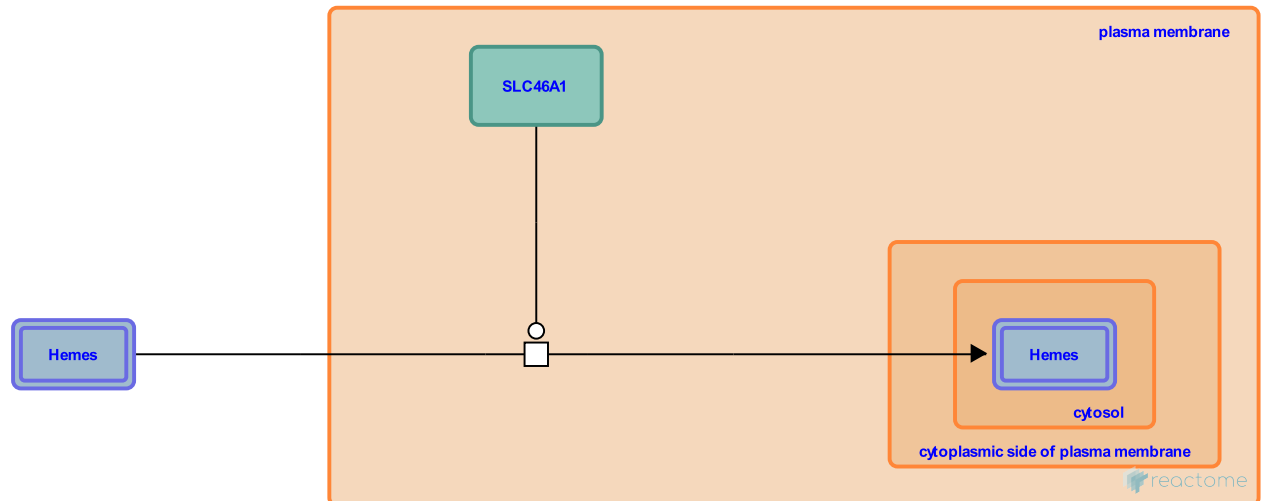
Location: [Heme signaling](#)

Stable identifier: R-RNO-917870

Type: transition

Compartments: plasma membrane

Inferred from: [SLC46A1 transports hemes from extracellular region 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>

PGRMC2 binds Hemes ↗

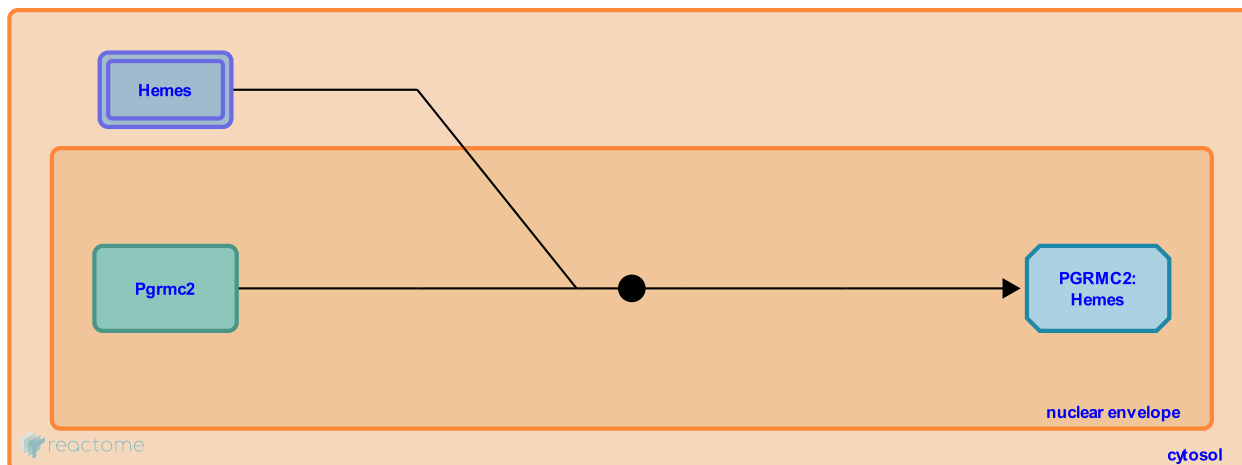
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707683

Type: binding

Compartments: nuclear envelope, cytosol

Inferred from: [PGRMC2 binds Hemes \(Homo sapiens\)](#)



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: [PGRMC2:Hemes translocate to the nucleus](#)

PGRMC2:Hemes translocate to the nucleus ↗

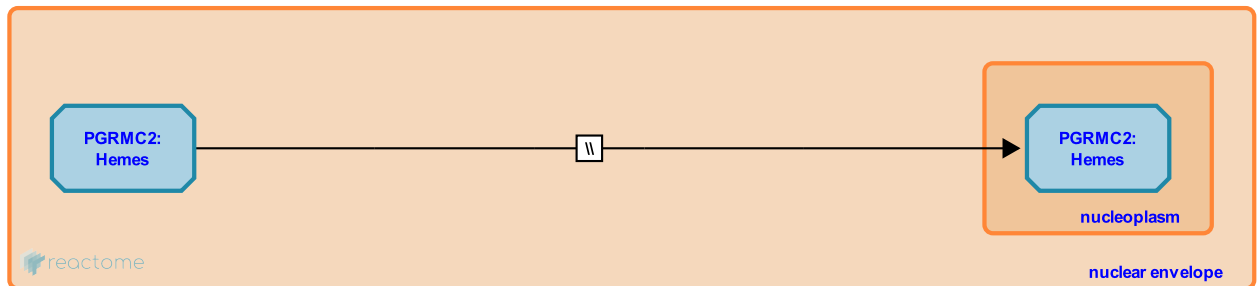
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707606

Type: omitted

Compartments: nuclear envelope, nucleoplasm

Inferred from: [PGRMC2:Hemes translocate to the nucleus \(Homo sapiens\)](#)



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: [PGRMC2 binds Hemes](#)

Followed by: [PGRMC2:Hemes dissociates](#)

PGRMC2:Hemes dissociates ↗

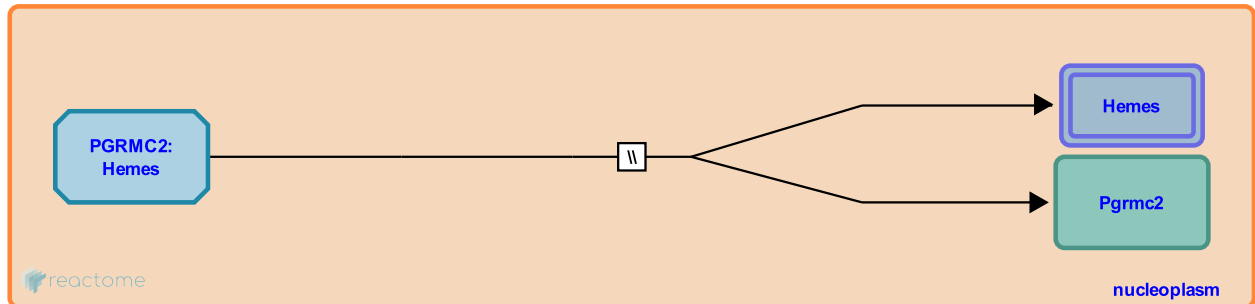
Location: [Heme signaling](#)

Stable identifier: R-RNO-9707856

Type: omitted

Compartments: nucleoplasm

Inferred from: [PGRMC2:Hemes dissociates \(Homo sapiens\)](#)



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: [PGRMC2:Hemes translocate to the nucleus](#)

XPO1 (CRM1) binds to BACH1:Hemes ↗

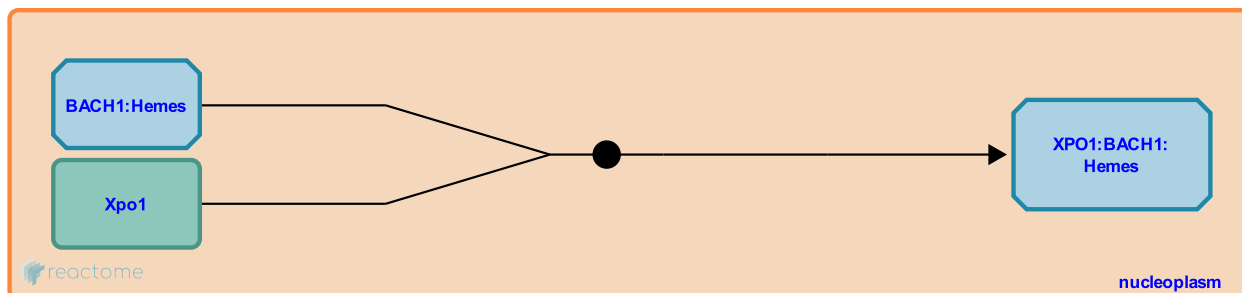
Location: [Heme signaling](#)

Stable identifier: R-RNO-9708430

Type: binding

Compartments: nucleoplasm

Inferred from: [XPO1 \(CRM1\) binds to BACH1:Hemes \(Homo sapiens\)](#)



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: [XPO1:BACH1:Hemes are transported out of the nucleus](#)

XPO1:BACH1:Hemes are transported out of the nucleus ↗

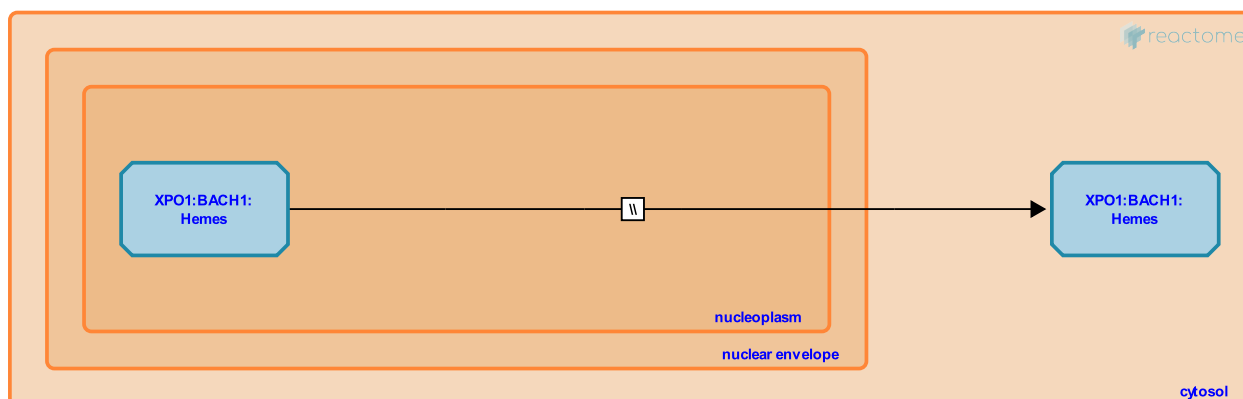
Location: [Heme signaling](#)

Stable identifier: R-RNO-9708423

Type: omitted

Compartments: nucleoplasm, cytosol

Inferred from: [XPO1:BACH1:Hemes are transported out of the nucleus \(Homo sapiens\)](#)



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: [XPO1 \(CRM1\) binds to BACH1:Hemes](#)

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