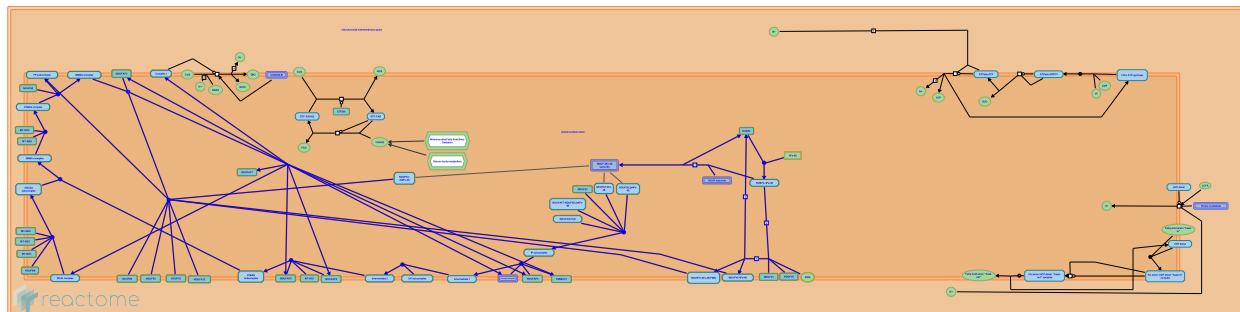


# Complex I biogenesis



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

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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. [↗](#)
- 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. [↗](#)

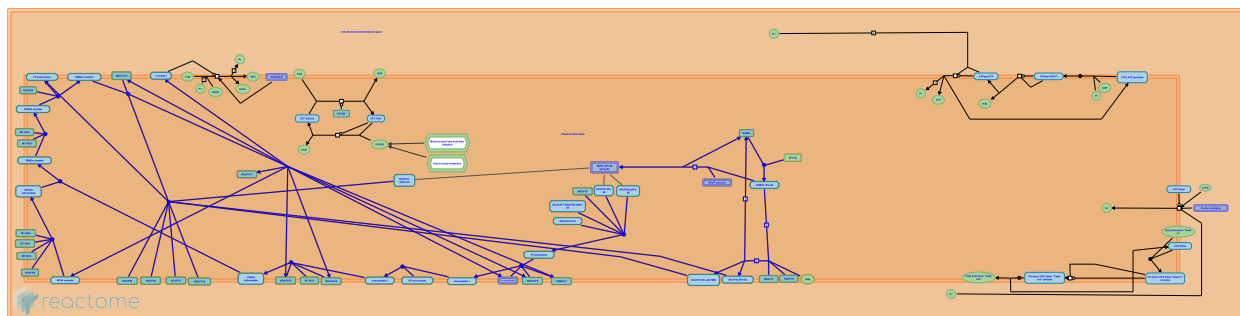
Reactome database release: 70

This document contains 1 pathway and 13 reactions ([see Table of Contents](#))

## Complex I biogenesis ↗

**Stable identifier:** R-DRE-6799198

**Inferred from:** [Complex I biogenesis \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

## NUBPL binds 4Fe-4S ↗

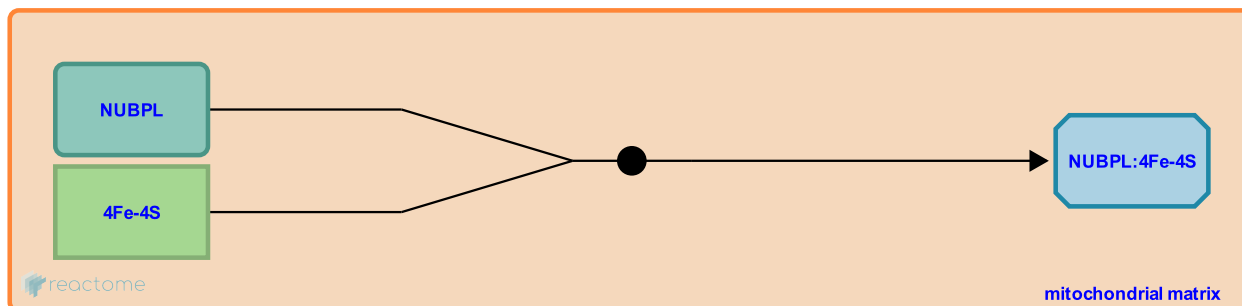
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-5690023

**Type:** binding

**Compartments:** mitochondrial matrix

**Inferred from:** [NUBPL binds 4Fe-4S \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Followed by:** [NUBPL transfers 4Fe-4S to Complex I subunits](#), [NUBPL transfers 4Fe-4S to NDUFV1, V2](#)

## NUBPL transfers 4Fe-4S to Complex I subunits ↗

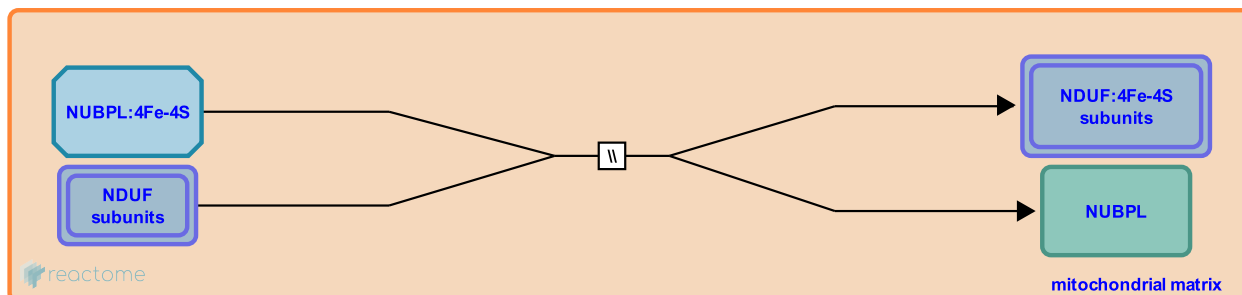
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6788523

**Type:** omitted

**Compartments:** mitochondrial matrix

**Inferred from:** [NUBPL transfers 4Fe-4S to Complex I subunits \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [NUBPL binds 4Fe-4S](#)

**Followed by:** [NDUF subunits bind to form the IP subcomplex](#), [NDUF subunits bind to form the FP subcomplex](#)

## NUBPL transfers 4Fe-4S to NDUFV1, V2 ↗

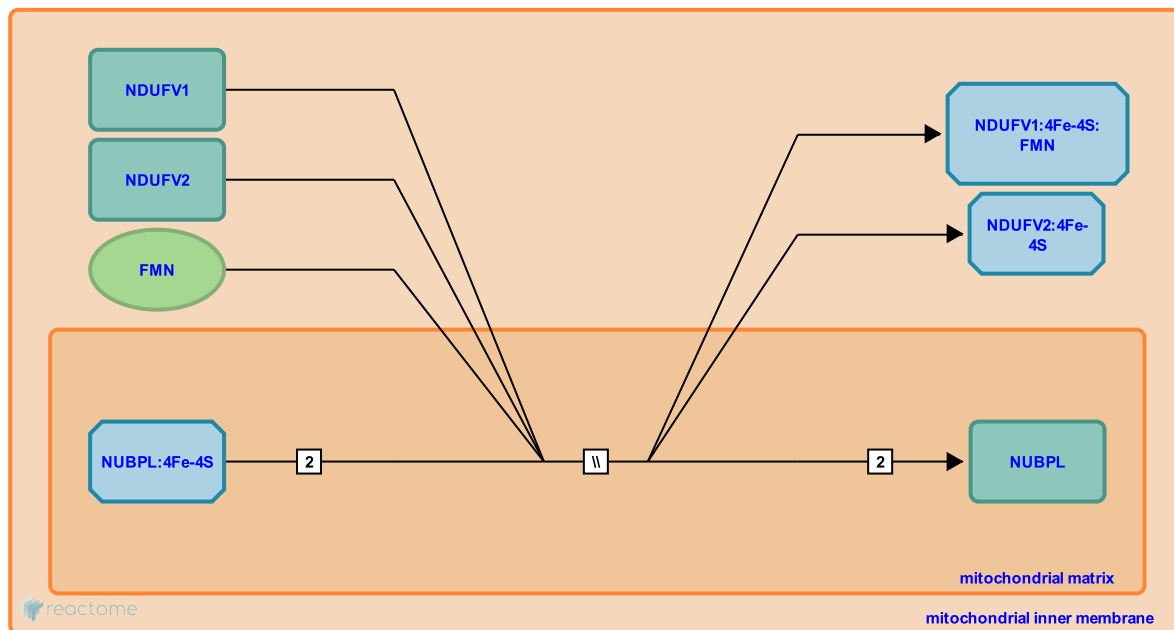
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6788556

**Type:** omitted

**Compartments:** mitochondrial matrix, mitochondrial inner membrane

**Inferred from:** [NUBPL transfers 4Fe-4S to NDUFV1, V2 \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [NUBPL binds 4Fe-4S](#)

**Followed by:** [NDUF subunits bind to form the FP subcomplex](#)

## NDUF subunits bind to form the IP subcomplex ↗

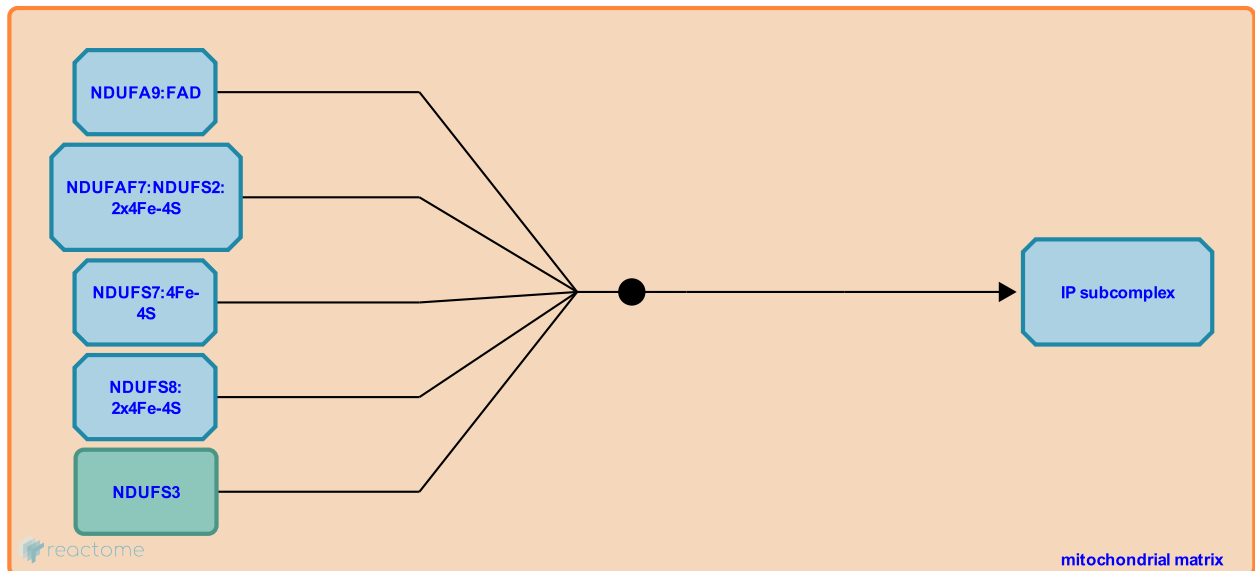
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6800868

**Type:** binding

**Compartments:** mitochondrial matrix

**Inferred from:** [NDUF subunits bind to form the IP subcomplex \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [NUBPL transfers 4Fe-4S to Complex I subunits](#)

**Followed by:** [IP subcomplex binds NDUFAF3, NDUFAF4, TIMMDC1 to form Intermediate 1](#)

## IP subcomplex binds NDUFAF3, NDUFAF4, TIMMDC1 to form Intermediate 1 [↗](#)

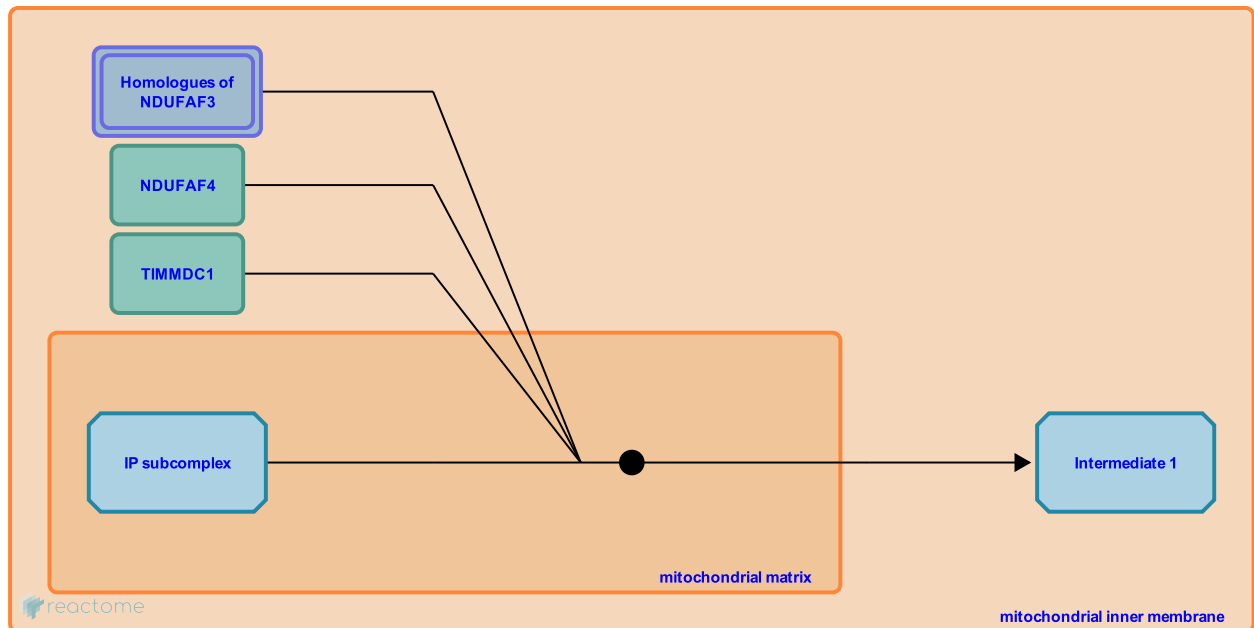
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6799203

**Type:** binding

**Compartments:** mitochondrial matrix, mitochondrial inner membrane

**Inferred from:** [IP subcomplex binds NDUFAF3, NDUFAF4, TIMMDC1 to form Intermediate 1 \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [NDUF subunits bind to form the IP subcomplex](#)

**Followed by:** [Intermediate 1 binds HP subcomplex to form Intermediate 2](#)



## Intermediate 1 binds HP subcomplex to form Intermediate 2 [↗](#)

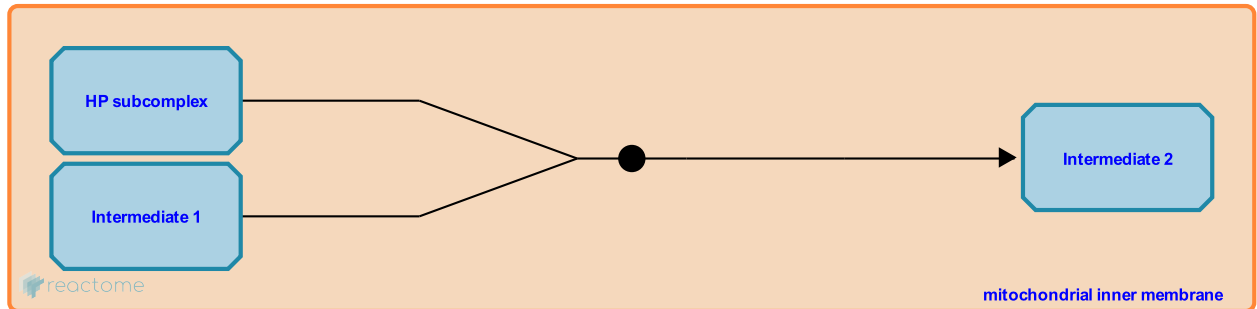
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6799178

**Type:** binding

**Compartments:** mitochondrial inner membrane

**Inferred from:** [Intermediate 1 binds HP subcomplex to form Intermediate 2 \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [IP subcomplex binds NDUFAF3, NDUFAF4, TIMMDC1 to form Intermediate 1](#)

**Followed by:** [Intermediate 2 binds MT-ND1:NDUFAF5:NDUFAF6 to form a 315kDa subcomplex](#)

## Intermediate 2 binds MT-ND1:NDUFAF5:NDUFAF6 to form a 315kDa subcomplex ↗

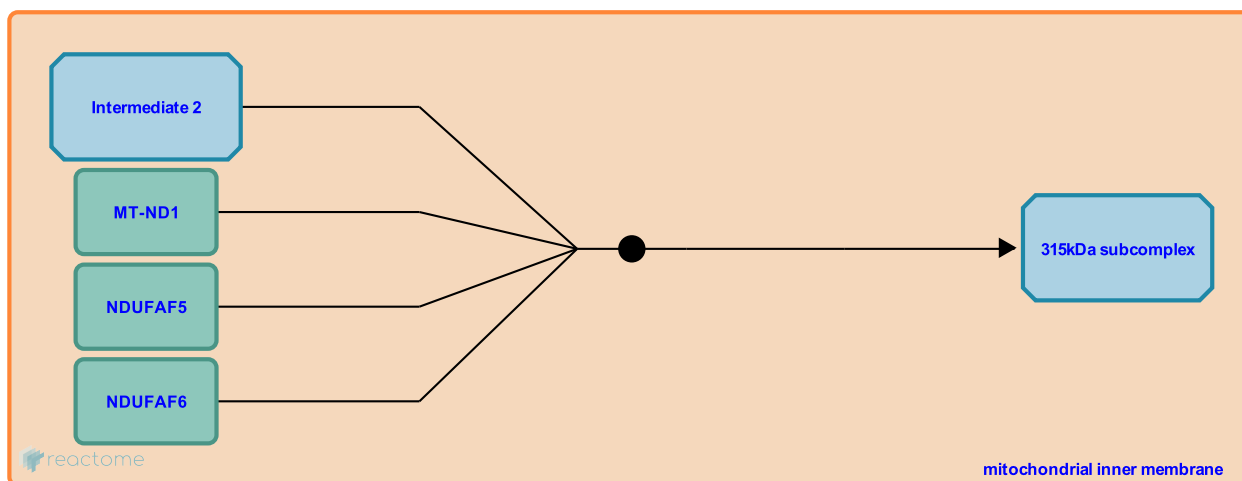
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6799191

**Type:** binding

**Compartments:** mitochondrial inner membrane

**Inferred from:** [Intermediate 2 binds MT-ND1:NDUFAF5:NDUFAF6 to form a 315kDa subcomplex \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [Intermediate 1 binds HP subcomplex to form Intermediate 2](#)

**Followed by:** [ND2, ND3, ND6, NDUFB6 bind the MCIA complex to form a 370kDa subcomplex](#)

## ND2, ND3, ND6, NDUFB6 bind the MCIA complex to form a 370kDa subcomplex ↗

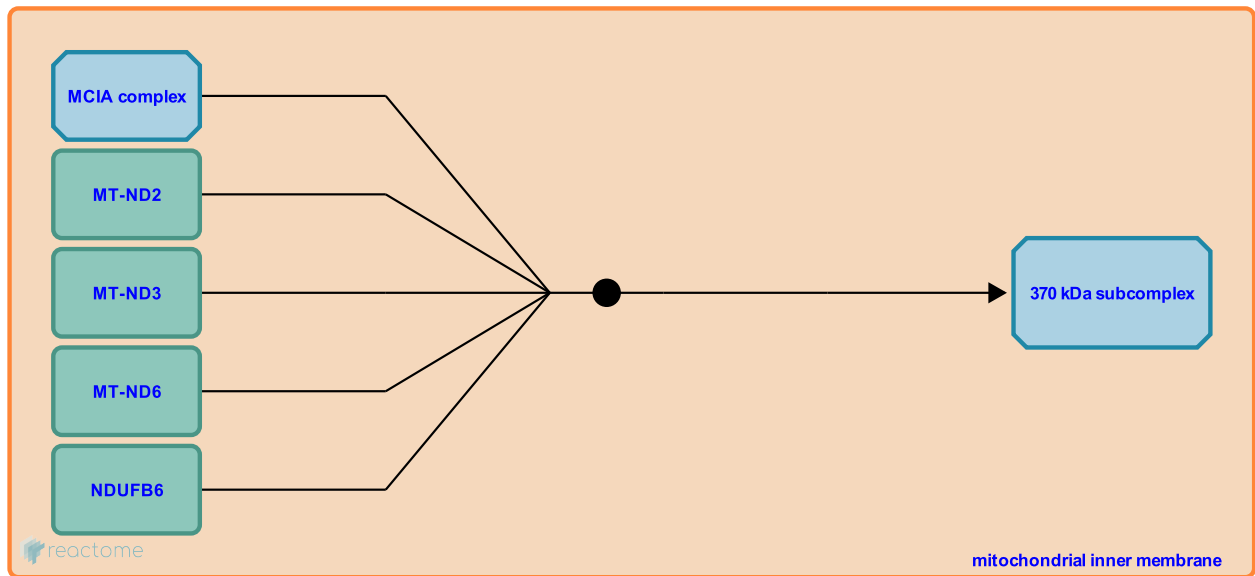
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6799199

**Type:** binding

**Compartments:** mitochondrial inner membrane

**Inferred from:** [ND2, ND3, ND6, NDUFB6 bind the MCIA complex to form a 370kDa subcomplex \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [Intermediate 2 binds MT-ND1:NDUF5:NDUF6 to form a 315kDa subcomplex](#)

**Followed by:** [The 315kDa subcomplex binds the 370kDa subcomplex to form the 550kDa complex](#)

## The 315kDa subcomplex binds the 370kDa subcomplex to form the 550kDa complex



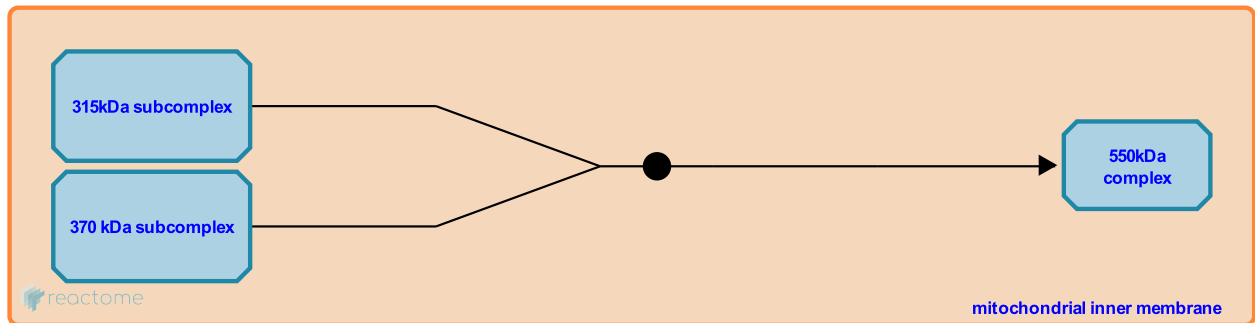
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6799202

**Type:** binding

**Compartments:** mitochondrial inner membrane

**Inferred from:** [The 315kDa subcomplex binds the 370kDa subcomplex to form the 550kDa complex \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [ND2, ND3, ND6, NDUFB6 bind the MCIA complex to form a 370kDa subcomplex](#)

**Followed by:** [ND4, ND5 bind the 550kDa complex to form the 815kDa complex](#)

## ND4, ND5 bind the 550kDa complex to form the 815kDa complex ↗

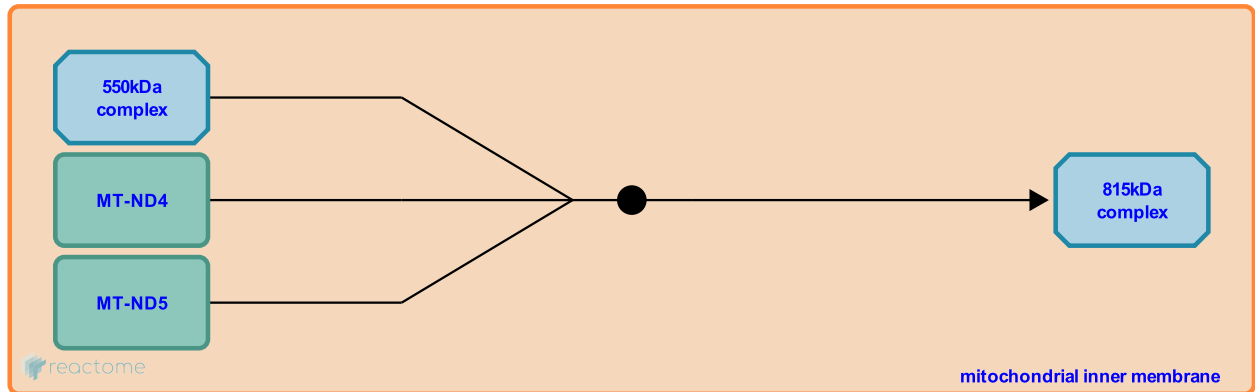
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6799197

**Type:** binding

**Compartments:** mitochondrial inner membrane

**Inferred from:** [ND4, ND5 bind the 550kDa complex to form the 815kDa complex \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [The 315kDa subcomplex binds the 370kDa subcomplex to form the 550kDa complex](#)

**Followed by:** [Peripheral arm subunits bind the 815kDa complex to form a 980kDa complex](#)

## NDUF subunits bind to form the FP subcomplex ↗

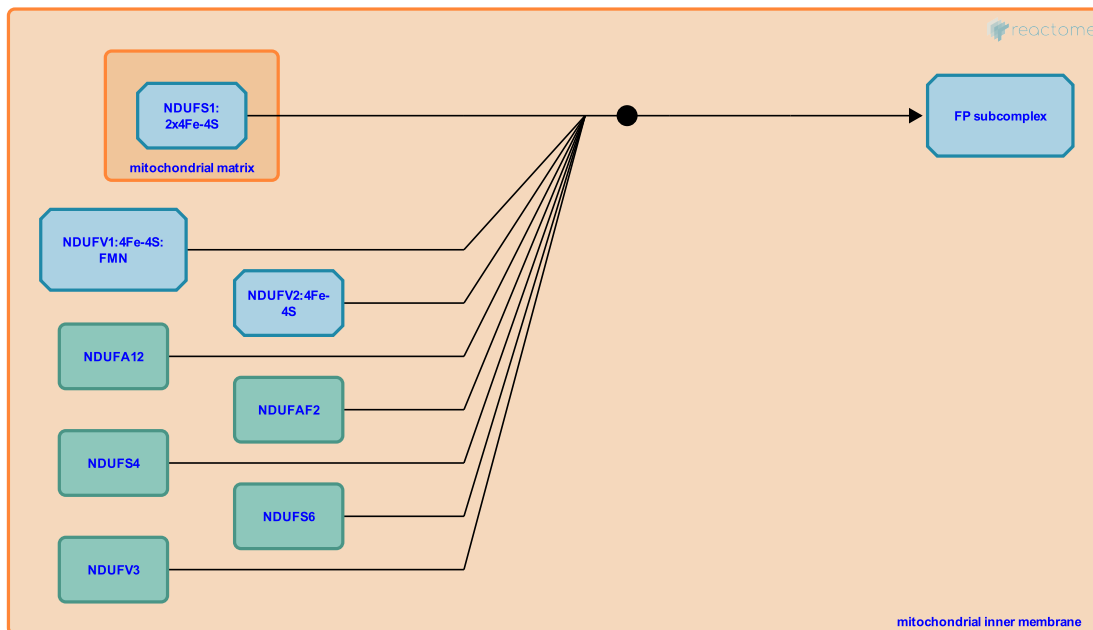
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6800870

**Type:** binding

**Compartments:** mitochondrial inner membrane, mitochondrial matrix

**Inferred from:** [NDUF subunits bind to form the FP subcomplex \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [NUBPL transfers 4Fe-4S to Complex I subunits](#), [NUBPL transfers 4Fe-4S to NDUFV1, V2](#)

**Followed by:** [Peripheral arm subunits bind the 815kDa complex to form a 980kDa complex](#)

## Peripheral arm subunits bind the 815kDa complex to form a 980kDa complex ↗

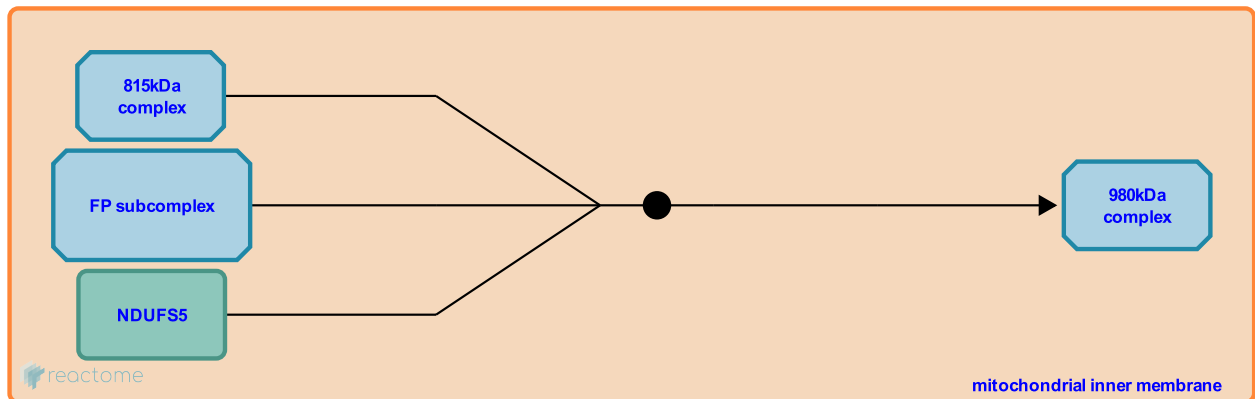
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6799179

**Type:** binding

**Compartments:** mitochondrial inner membrane

**Inferred from:** [Peripheral arm subunits bind the 815kDa complex to form a 980kDa complex \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [ND4, ND5 bind the 550kDa complex to form the 815kDa complex](#), [NDUF subunits bind to form the FP subcomplex](#)

**Followed by:** [The MCIA complex, NDUFAF2-7 all dissociate from the 980kDa complex, resulting in Complex I](#)

## The MCIA complex, NDUFAF2-7 all dissociate from the 980kDa complex, resulting in Complex I ↗

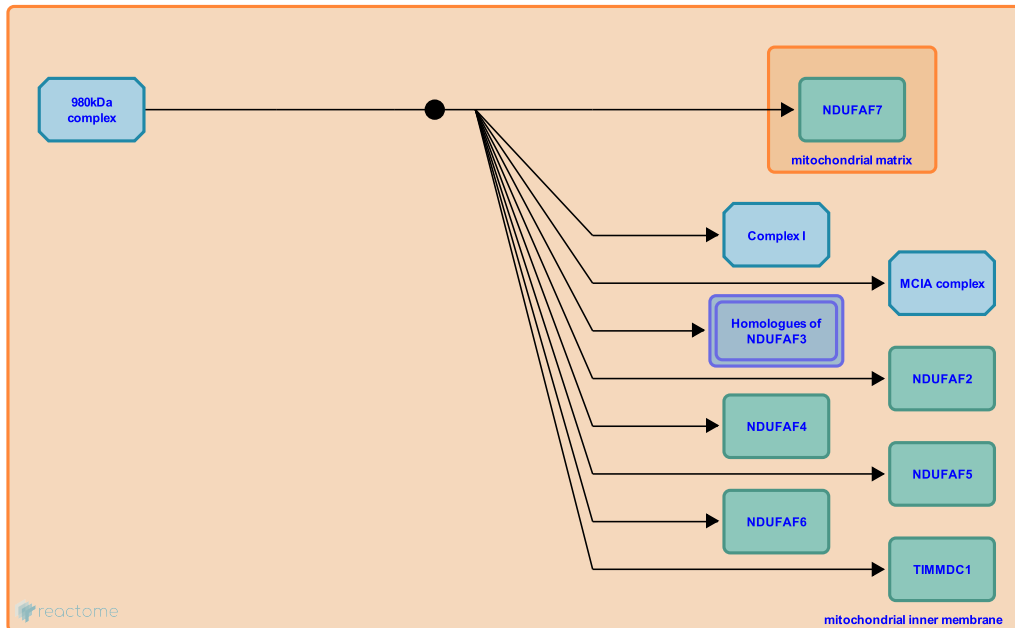
**Location:** [Complex I biogenesis](#)

**Stable identifier:** R-DRE-6799196

**Type:** dissociation

**Compartments:** mitochondrial inner membrane

**Inferred from:** [The MCIA complex, NDUFAF2-7 all dissociate from the 980kDa complex, resulting in Complex I \(Homo sapiens\)](#)



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.](/electronic_inference_compara.html) For details on PANTHER see also: <http://www.pantherdb.org/about.jsp>

**Preceded by:** [Peripheral arm subunits bind the 815kDa complex to form a 980kDa complex](#)



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