Mitochondrial iron-sulfur cluster biogenesis

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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.

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Literature references


Reactome database release: 79

This document contains 2 pathways and 4 reactions (see Table of Contents)
Mitochondrial iron-sulfur cluster biogenesis

Stable identifier: R-HSA-1362409

Compartments: mitochondrial inner membrane, mitochondrial matrix, mitochondrial intermembrane space

Iron-sulfur (Fe-S) proteins are localized in the cytosol, nucleus, and mitochondria of mammalian cells (reviewed in Stemmler et al. 2010, Rouault 2012, Bandyopadhyay et al. 2008, Lill 2009, Lill et al. 2012). Fe-S protein biogenesis in the mitochondrial matrix involves the iron-sulfur cluster (ISC) assembly machinery. Ferrous iron is transported across the inner mitochondrial membrane into the mitochondrial matrix by Mitoferrin-1 (SLC25A37) and Mitoferrin-2 (SLC25A28). (Mitoferrin-1 is enriched in erythroid cells while Mitoferrin-2 is ubiquitous.) Frataxin binds ferrous iron in the mitochondrial matrix. The cysteine desulfurase NFS1 in a subcomplex with ISD11 provides the sulfur by converting cyteine into alanine and forming a persulfide which is used for cluster formation on ISCU, the scaffold protein. Interaction between NFS1 and ISD11 is necessary for desulfurase activity. Frataxin binds to a complex containing NFS1, ISD11, and ISCU and is proposed to function as an iron donor to ISCU or as an allosteric switch that activates sulfur transfer and Fe-S cluster assembly (Tsai and Barondeau 2010). Cluster formation also involves the electron transfer chain ferredoxin reductase and ferredoxin. ISCU initially forms clusters containing 2 iron atoms and 2 sulfur atoms ([2Fe-2S] clusters). They are released by the function of HSP70-HSC20 chaperones and the monothiol glutaredoxin GLRX5 and used for assembly of [2Fe-2S] proteins. Assembly of larger clusters such as [4Fe-4S] clusters may involve the function of ISCA1, ISCA2, and IBA57. The clusters are transferred to apo-enzymes such as the respiratory complexes, aconitase, and lipoate synthase through dedicated targeting factors such as IND1, NFU1, and BOLA3.

Literature references


**Editions**

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Mitoferrin translocates iron from the mitochondrial intermembrane space to the mitochondrial matrix

**Location:** Mitochondrial iron-sulfur cluster biogenesis

**Stable identifier:** R-HSA-1362417