FXN:NFS1:ISD11:ISCU assembles 2Fe-2S iron-sulfur cluster

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04/05/2024

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).

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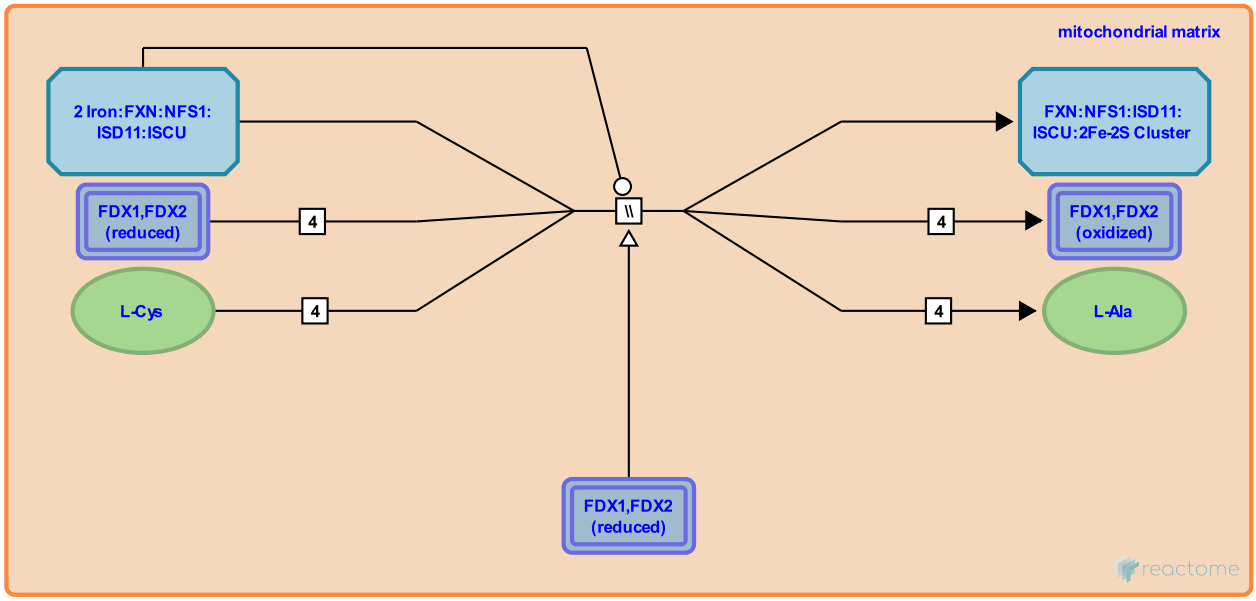
Stable identifier: R-HSA-1362408

Type: omitted

Compartments: mitochondrial matrix



Iron-sulfur clusters are assembled on the scaffold, ISCU. Based on homology with bacterial IscU:IscS complexes (reviewed in Johnson et al. 2005), one molecule of ISCU is bound to each subunit of a NFS1 dimer (Marinoni et al. 2012). A single complex may thus be capable of assembling two 2Fe-2S clusters. Sulfide is provided by desulfuration of cysteine by NFS1:ISD11 (Biederbick et al. 2006, Shi et al. 2009, Tsai and Barondeau 2010). It has been proposed that ferrous iron is delivered by FXN (Gerber et al. 2003, Yoon and Cowan 2003, Schmucker et al. 2011) bound to ISCU (inferred from yeast, Wang and Craig 2008), although more recent studies suggested that FXN functions as an allosteric effector to stimulate sulfide transfer (Tsai et al. 2010). Holo-ISCU (ISCU bound to a newly synthesized 2Fe-2S cluster) transiently interacts with a dedicated HSP70 chaperone system including Mortalin (GRP75) and HSP20 and GLRX5 (GRX5). Electrons supplied by FDX2 (FDX1L) are required (Tong et al. 2003, Cai et al. 2017) and may reduce the sulfur from S0 to S2- (sulfide). NFU1 binds an Fe-S cluster (Tong et al. 2003, inferred from bacteria Yuvaniyama et al. 2000) and, from biochemical studies of bacterial NFU1 homologues, is proposed to be an intermediate Fe-S cluster carrier (Bandyopadhy et al. 2008). Mutations in human NFU1 affect only a subset of Fe-S proteins (Navarro-Sastre et al. 2011).

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Editions

2011-06-04	Authored, Edited	May, B.
2012-09-24	Authored	Lill, R.
2012-10-12	Reviewed	Rouault, TA., Tong, WH.