Defective CP causes aceruloplasminemia

(ACERULOP)

Broer, S., Jassal, B.

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 Creative Commons Attribution 4.0 International (CC BY 4.0) License. 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.

25/12/2022

https://reactome.org
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


Reactome database release: 83

This document contains 1 pathway and 1 reaction (see Table of Contents)
Defective CP causes aceruloplasminemia (ACERULOP)

Stable identifier: R-HSA-5619060

Diseases: aceruloplasminemia

Ceruloplasmin (CP), synthesised in the liver and secreted into plasma, is a copper-binding (6-7 atoms per molecule) glycoprotein involved in iron trafficking in vertebrates. CP is essential for SLC40A1 (ferroportin) stability at the cell surface, the protein that mediates iron efflux from cells. CP also possesses ferroxidase activity, which oxidises ferrous iron (Fe2+) to ferric iron (Fe3+) following its transfer out of the cell. Fe3+ can then be loaded on to extracellular transferrin which transports it around the body to sites where it is required. Iron is vital for many metabolic processes such as electron transport and the transport and storage of oxygen.

Defects in CP (or indeed SLC40A1) can lead to the phenotype of iron overload as seen in the disorder aceruloplasminemia (ACERULOP; MIM:604290). It is a rare autosomal recessive disorder of iron metabolism characterised by iron accumulation mainly in the brain, but also in liver, pancreas and retina. Patients develop retinal degeneration, diabetes mellitus and neurological disturbance. ACERULOP belongs to a group of disorders known as NBIA (neurodegeneration with brain iron accumulation), distinguishing it from hereditary hemochromatosis (serum iron is high but the brain is usually not affected) and from disorders of copper metabolism such as Menkes and Wilson disease (Harris et al. 1995, Kono 2012, Musci et al. 2014).

Literature references


Defective CP does not oxidise Fe2+ to Fe3+

Location: Defective CP causes aceruloplasminemia (ACERULOP)

Stable identifier: R-HSA-5621402

Type: transition

Compartments: plasma membrane, extracellular region

Diseases: aceruloplasminemia

Ceruloplasmin (CP), synthesised in the liver and secreted into plasma, is a copper-binding (6-7 atoms per molecule) glycoprotein involved in iron trafficking in vertebrates. CP is essential for SLC40A1 (ferroportin) stability at the cell surface, the protein that mediates iron efflux from cells. CP also possesses ferroxidase activity, which oxidises ferrous iron (Fe2+) to ferric iron (Fe3+) following its transfer out of the cell. Defects in CP (or indeed SLC40A1) can lead to the phenotype of iron overload as seen in the disorder aceruloplasminemia (ACERULOP; MIM:604290). It is a rare autosomal recessive disorder of iron metabolism characterised by iron accumulation mainly in the brain, but also in liver, pancreas and retina. Patients develop retinal degeneration, diabetes mellitus and neurological disturbance.

Mutations that can cause ACERULOP include W858*, E797Rfs*12, D411Tfs*36 and 778fs*12 (Takahashi et al. 1996, Logan et al. 1994, Okamoto et al. 1996, Harris et al. 1995).

**Literature references**


https://reactome.org
<table>
<thead>
<tr>
<th>Editions</th>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2014-08-29</td>
<td>Authored, Edited</td>
<td>Jassal, B.</td>
</tr>
<tr>
<td></td>
<td>2015-08-04</td>
<td>Reviewed</td>
<td>Broer, S.</td>
</tr>
</tbody>
</table>
Table of Contents

Introduction 1

* Defective CP causes aceruloplasminemia (ACERULOP) 2
  * Defective CP does not oxidise Fe2+ to Fe3+ 4

Table of Contents 6