Class I peroxisomal membrane protein import

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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.

17/11/2022
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: 82

This document contains 1 pathway and 6 reactions (see Table of Contents)
Most peroxisomal membrane proteins (PMPs) are inserted into the peroxisomal membrane by the receptor-chaperone PEX19 and the docking receptor PEX3 (Soukupova et al. 1999, Muntau et al. 2003, Fang et al. 2004, Fujiki et al. 2006, Matsuzono and Fujiki 2006, Matsuzono et al. 2006, Pinto et al. 2006, Sato et al. 2008, Sato et al. 2010, Schmidt et al. 2010, Hattula et al. 2014, reviewed in Fujiki et al. 2014, Mayerhofer 2016). PEX19 binds the PMP as it is translated in the cytosol. Recognition of the PMP by PEX19 appears to depend on positively charged residues in the transmembrane domain of the PMP (Costello et al. 2017). The PEX19:PMP complex then interacts with PEX3 located in the peroxisomal membrane. Through a mechanism that is not yet clear, the PMP is inserted into the peroxisomal membrane and PEX19 dissociates from PEX3. A current model involves transfer of the PMP from PEX19 to a hydrophobic region of PEX3 followed by insertion of the PMP into the membrane (Chen et al. 2014, reviewed by Giannopoulou et al. 2016). The process does not appear to require hydrolysis of ATP or GTP (Pinto et al. 2006).

Unlike other PMPs, PEX3 is inserted into the peroxisomal membrane by binding PEX19 and then docking with PEX16 (Matsuzaki and Fujiki 2008). Both PEX3 and PEX16 can also be co-translationally inserted into the endoplasmic reticulum membrane (Kim et al. 2006, Yonekawa et al. 2011, Aranovich et al. 2014, Hua et al. 2015, Mayerhofer et al. 2016). This region of the ER membrane then buds to contribute to new peroxisomes. PEX3 is also observed to insert into the mitochondrial outer membrane (Sugiura et al. 2017). Regions of the ER membrane and mitochondrial outer membrane are then released to form pre-peroxisomal vesicles which fuse to form new peroxisomes (Sugiura et al. 2017). Peroxisomes therefore appear to arise from fission of existing peroxisomes and production of new peroxisomes from precursors derived from mitochondria and the ER (Sugiura et al. 2017, reviewed in Fujiki et al. 2014, Hua and Kim 2016).
Literature references


Editions

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PEX19 binds class I peroxisomal membrane proteins

**Location:** Class I peroxisomal membrane protein import

**Stable identifier:** R-HSA-9603804

**Type:** binding

**Compartments:** cytosol

In the cytosol, PEX19 binds newly synthesized class I peroxisomal membrane proteins (Sacksteder et al. 2000, Fransen et al. 2001, Jones et al. 2004, reviewed in Fujiki et al. 2006). The C-terminal region and a conserved N-terminal helical segment of PEX19 bind to peroxisomal membrane proteins (Fransen et al. 2005, Schueller et al. 2010) and PEX19 acts both as a chaperone and as an import receptor (Jones et al. 2004). PEX19 is farnesylated (Görte et al. 1998, Sacksteder et al. 2000, Vastiau et al. 2006) and the farnesyl group is buried in a hydrophobic cavity which alters the conformation of PEX19 to yield two hydrophobic pockets involved in binding peroxisomal membrane proteins (Emmanouilidis et al. 2017). The number of positively charged amino acid residues in the transmembrane domain of the PMP appears to determine binding by PEX19 and, hence, targeting to the peroxisomal membrane protein (Costello et al. 2017).


**Followed by:** PEX19:class I PMP binds PEX3

**Literature references**


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https://reactome.org
PEX19: class I PMP binds PEX3

Location: Class I peroxisomal membrane protein import

Stable identifier: R-HSA-9603784

Type: binding

Compartments: peroxisomal membrane


Preceded by: PEX19 binds class I peroxisomal membrane proteins

Followed by: PEX3:PEX19:class I PMP dissociates

Literature references


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The PEX19:PEX3:peroxisomal membrane protein complex dissociates, yielding cytosolic PEX19, membrane-bound PEX3, and the peroxisomal membrane protein inserted in the peroxisomal membrane (Fang et al. 2004, Matsuzono and Fujiki 2006, Schueller et al. 2010, Chen et al. 2014, reviewed in Fujiki et al. 2006). The mechanism of the reaction is not fully characterized. One current model posits the transfer of the peroxisomal membrane protein from a hydrophobic region of PEX19 to a hydrophobic region of PEX3 followed by intervention in the membrane layer to release the peroxisomal membrane protein into the membrane bilayer (Chen et al. 2014). An amphipathic helical segment in the N-terminal region of PEX19 may compete with the peroxisomal membrane protein for a binding site in the C-terminal region of PEX19 and thereby participate in the release of the peroxisomal membrane protein from PEX19 (Schueller et al. 2010).

**Preceded by:** PEX19:class I PMP binds PEX3

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**PEX19 binds PEX3**

**Location:** Class I peroxisomal membrane protein import

**Stable identifier:** R-HSA-9603801

**Type:** binding

**Compartments:** cytosol

**Inferred from:** PEX19 binds Pex3 (Homo sapiens)

In the cytosol, PEX19 binds to newly translated PEX3 (inferred from human PEX19 binding rat Pex3). PEX19 binds the C-terminal region of PEX3 and the membrane targeting signal of PEX3 is located in the N-terminal region (Soukupova et al. 1999, Fransen et al. 2001, Fransen et al. 2005).

**Followed by:** PEX19:PEX3 binds PEX16

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[https://reactome.org](https://reactome.org)
**PEX19:PEX3 binds PEX16**

**Location:** Class I peroxisomal membrane protein import

**Stable identifier:** R-HSA-9603797

**Type:** binding

**Compartments:** peroxisomal membrane

**Inferred from:** PEX19:Pex3 binds PEX16 (Homo sapiens)

The cytosolic PEX19:PEX3 complex binds PEX16 located in the peroxisomal membrane (inferred from human PEX19, human PEX16, and rat Pex3). Thus PEX16 serves as a docking factor. PEX3 is believed to be inserted in the peroxisomal membrane by this pathway and by direct co-translational insertion in the membrane of the endoplasmic reticulum that then buds to generate peroxisomes.

**Preceded by:** PEX19 binds PEX3

**Followed by:** PEX16:PEX19:PEX3 dissociates

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PEX16:PEX19:PEX3 dissociates

Location: Class I peroxisomal membrane protein import

Stable identifier: R-HSA-9603791

Type: dissociation

Compartments: peroxisomal membrane

Inferred from: PEX16:PEX19:Pex3 dissociates (Homo sapiens)

The PEX16:PEX19:PEX3 complex dissociates, yielding cytosolic PEX19 and PEX3 and PEX16 inserted in the membrane (inferred from human PEX16, human PEX19, and rat PEX3).

Preceded by: PEX19:PEX3 binds PEX16

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</table>
Table of Contents

Introduction 
- Class I peroxisomal membrane protein import 1
  - PEX19 binds class I peroxisomal membrane proteins 2
  - PEX19: class I PMP binds PEX3 4
  - PEX3:PEX19: class I PMP dissociates 6
  - PEX19 binds PEX3 8
  - PEX19:PEX3 binds PEX16 9
  - PEX16:PEX19:PEX3 dissociates 10

Table of Contents 12