PEX2:PEX10:PEX12 monoubiquitinates PEX5S,L at cysteine-11

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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

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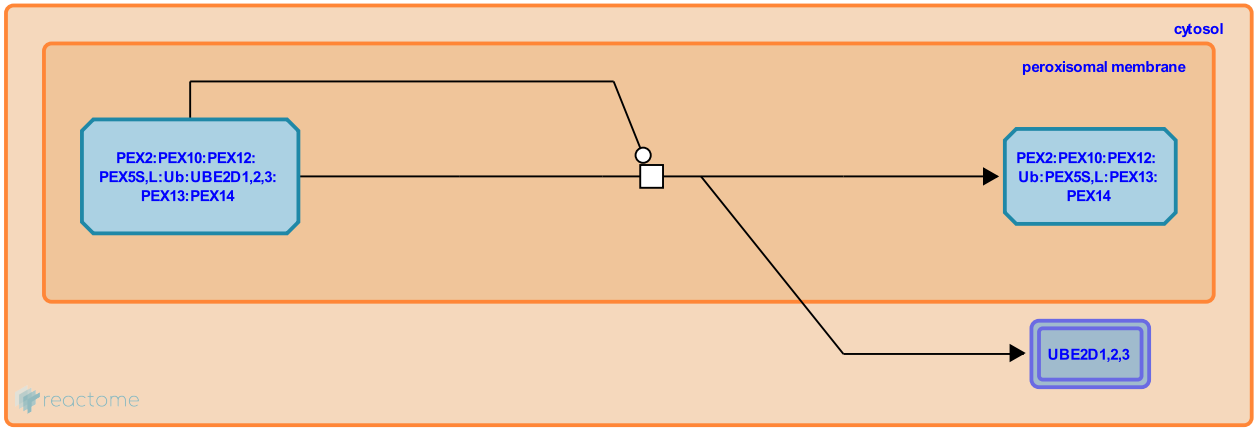
Stable identifier: R-HSA-8953946

Type: transition

Compartments: peroxisomal membrane



The RING-type E3 ubiquitin ligase sub-complex PEX2:PEX10:PEX12 catalyzes the transfer of ubiquitin from an E2-ubiquitin conjugate (one of Ub:UBE2D1, Ub:UBE2D2, or Ub:UBE2D3) to the cysteine-11 residue of the substrate PEX5L, the peroxisomal matrix protein shuttling receptor (Carvalho et al. 2007; Grou et al. 2008, Okumoto et al. 2011, Sargent et al. 2016, inferred from yeast in Dodt and Gould 1996). The thiol ester bond between ubiquitin and the cysteine residue of PEX5 is unusual among ubiquitin substrates, which usually have isopeptide bonds between ubiquitin and a lysine residue. Monoubiquitination of PEX5 at cysteine-11 is an integral and mandatory step in the PEX5-mediated peroxisomal protein transport pathway; in its absence, PEX5 cannot be extracted from the peroxisomal membrane docking/translocation machinery (the peroxisomal protein translocon), and thus transport of newly synthesized peroxisomal matrix proteins to the organelle matrix stops (Grou et al. 2009). In addition to monoubiquitinating PEX5 during peroxisomal protein import, the PEX2:PEX10:PEX12 complex has also been implicated in pexophagy, a type of selective autophagy targeting peroxisomes. Pexophagy seems to be triggered mainly by ubiquitination of PEX5, which, in this case, can occur either at its cysteine-11 or lysine-209 residues, but ubiquitination of ABCD3 (also known as PMP70) and other peroxisomal membrane proteins may also be involved (Zhang et al. 2015, inferred from mouse in Nordgren et al. 2015, Sargent et al. 2016).

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Editions

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