

# PEX1:PEX6:PEX26:ZFAND6 dissociates Ub:PEX5L and PEX7 from PEX14:PEX13:PEX2:PEX10:PEX12 and translocates PEX5L and PEX7 from the peroxisomal membrane to the cytosol

Azevedo, JE., Fransen, M., May, B., Van Veldhoven, PP.

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 <u>Creative Commons Attribution 4.0 International (CC BY 4.0)</u> <u>License</u>. For more information see our <u>license</u>.

19/05/2024

## 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).

#### Literature references

- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. 7
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. A
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, *14*, e1005968. *オ*

This document contains 1 reaction (see Table of Contents)

## PEX1:PEX6:PEX26:ZFAND6 dissociates Ub:PEX5L and PEX7 from PEX14:PEX13:PEX2:PEX10:PEX12 and translocates PEX5L and PEX7 from the peroxisomal membrane to the cytosol 7

Stable identifier: R-HSA-9033499

Type: uncertain

#### Compartments: peroxisomal membrane



Ubiquitinated PEX5 isoform L (Ub:PEX5L) is released from the peroxisomal membrane Docking and Translocation Module by PEX1:PEX6:PEX26 (the peroxisomal AAA ATPase complex, receptor export module) (Tamura et al. 2014, Law et al. 2017, also inferred from yeast homologs). PEX1 and PEX6 form a cytosolic hexameric ring that is anchored to the peroxisomal membrane by PEX26. Hydrolysis of ATP by PEX1 and PEX6 appears to cause a conformational change in PEX1:PEX6:PEX26 that removes Ub:PEX5L from the peroxisomal membrane and into the cytosol (reviewed in Saffert et al. 2017). ZFAND6 probably binds ubiquitinated PEX5 and PEX6 and acts as an export factor (Miyata et al. 2012). Export of PEX7 back to the cytosol requires export of PEX5L but PEX7 and PEX5L appear to be exported separately (Rodrigues et al. 2014).

#### Literature references

- Matsumoto, N., Takeba, R., Tamura, S., Fujiki, Y. (2014). AAA peroxins and their recruiter Pex26p modulate the interactions of peroxins involved in peroxisomal protein import. J. Biol. Chem., 289, 24336-46. 🛪
- Law, KB., Di Pietro, E., Moser, A., Jones, RO., Bronte-Tinkew, D., Braverman, N. et al. (2017). The peroxisomal AAA ATPase complex prevents pexophagy and development of peroxisome biogenesis disorders. *Autophagy*, *13*, 868-884. *¬*
- Miyata, N., Noguchi, M., Mukai, S., Okumoto, K., Fujiki, Y. (2012). AWP1/ZFAND6 functions in Pex5 export by interacting with cys-monoubiquitinated Pex5 and Pex6 AAA ATPase. *Traffic, 13,* 168-83.
- Rodrigues, TA., Grou, CP., Brites, P., Alencastre, IS., Azevedo, JE., Fransen, M. et al. (2014). A PEX7-centered perspective on the peroxisomal targeting signal type 2-mediated protein import pathway. *Mol. Cell. Biol.*, 34, 2917-28.
- Saffert, P., Wendler, P., Enenkel, C. (2017). Structure and Function of p97 and Pex1/6 Type II AAA+ Complexes. Front Mol Biosci, 4, 33. 7

# Editions

2017-12-20	Authored, Edited	May, B.
2018-02-13	Reviewed	Van Veldhoven, PP., Fransen, M.
2018-03-12	Reviewed	Azevedo, JE.