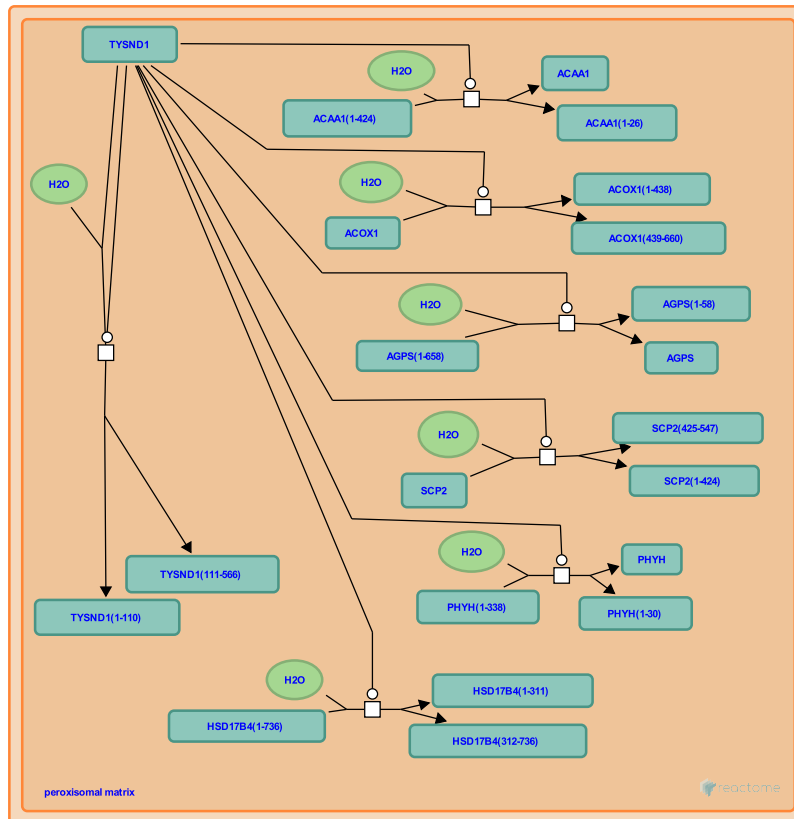


# TYSND1 cleaves peroxisomal proteins



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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](https://reactome.org/textbook/).

06/05/2024

## 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. [↗](#)
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- 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. [↗](#)

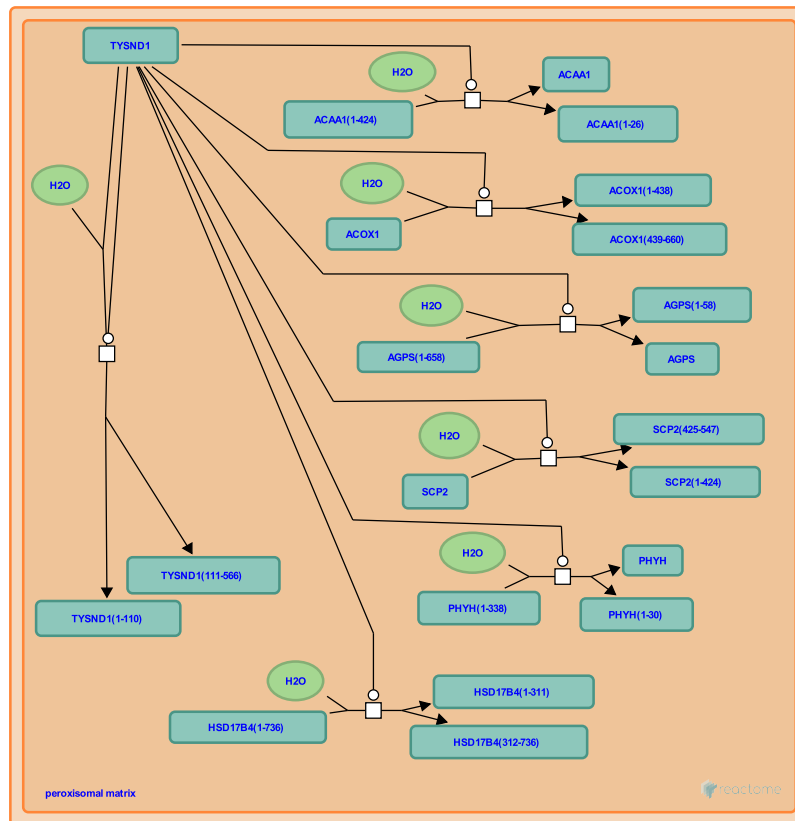
Reactome database release: 88

This document contains 1 pathway and 7 reactions ([see Table of Contents](#))

## TYSND1 cleaves peroxisomal proteins ↗

**Stable identifier:** R-HSA-9033500

**Compartments:** peroxisomal matrix



After proteins are imported into the peroxisome a subset of proteins are cleaved by the protease TYSD1 (Okumoto et al. 2011). Based on mutagenesis of human TYSD1 (Okumoto et al. 2011) and the homolog in Arabidopsis (Schuhmann et al. 2008), TYSD1 appears to be a trypsin-like serine protease containing a conserved histidine aspartate serine triad essential for catalysis. Mice lacking *Tysnd1* have reduced peroxisomal localization of some peroxisomal enzymes and exhibit reduced beta-oxidation of fatty acids and metabolism of phytanic acid (Mizuno et al. 2013). Male mice lacking *Tysnd1* are sterile due to sperm that lack acrosomal caps.

### Literature references

Kametani, Y., Okumoto, K., Fujiki, Y. (2011). Two proteases, trypsin domain-containing 1 (*Tysnd1*) and peroxisomal lon protease (*PsLon*), cooperatively regulate fatty acid  $\beta$ -oxidation in peroxisomal matrix. *J. Biol. Chem.*, 286, 44367-79. ↗

Alodaib, AN., Kurochkin, IV., Iwasa, H., Nishimukai, M., Okazaki, Y., Maeba, R. et al. (2013). *Tysnd1* deficiency in mice interferes with the peroxisomal localization of PTS2 enzymes, causing lipid metabolic abnormalities and male infertility. *PLoS Genet.*, 9, e1003286. ↗

Gietl, C., Adamska, I., Schuhmann, H., Huesgen, PF. (2008). The DEG15 serine protease cleaves peroxisomal targeting signal 2-containing proteins in Arabidopsis. *Plant Physiol.*, 148, 1847-56. ↗

### Editions

2017-12-22	Authored, Edited	May, B.
2018-02-13	Reviewed	Van Veldhoven, PP., Fransen, M.
2018-03-12	Reviewed	Azevedo, JE.

## TYSND1 cleaves ACAA1 ↗

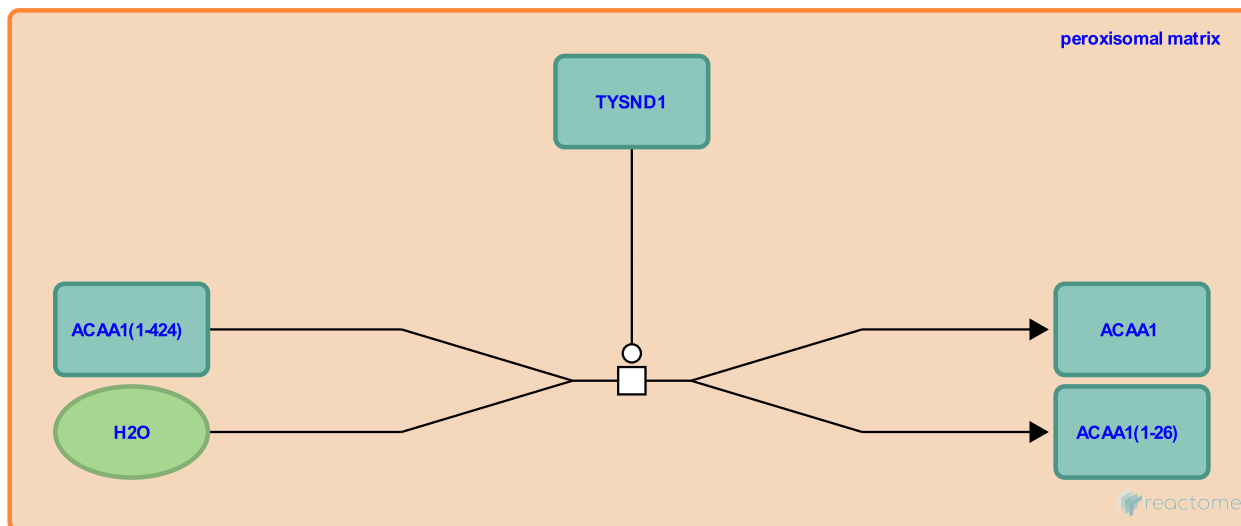
**Location:** [TYSND1 cleaves peroxisomal proteins](#)

**Stable identifier:** R-HSA-9033529

**Type:** transition

**Compartments:** peroxisomal matrix

**Inferred from:** [Tysnd1 cleaves Acaa1a \(Mus musculus\)](#)



The trypsin-like serine-type endopeptidase TYSD1 cleaves ACAA1 between amino acid residues 26 and 27, yielding ACAA1(1-26) and ACAA1(27-424) (Okumoto et al. 2011). In mice, knockout of *Tysnd1* causes reduced localization of *Acaa1* to the peroxisome.

### Literature references

Kametani, Y., Okumoto, K., Fujiki, Y. (2011). Two proteases, trypsin domain-containing 1 (*Tysnd1*) and peroxisomal ion protease (*PsLon*), cooperatively regulate fatty acid  $\beta$ -oxidation in peroxisomal matrix. *J. Biol. Chem.*, 286, 44367-79. ↗

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## TYSND1 cleaves ACOX1 ↗

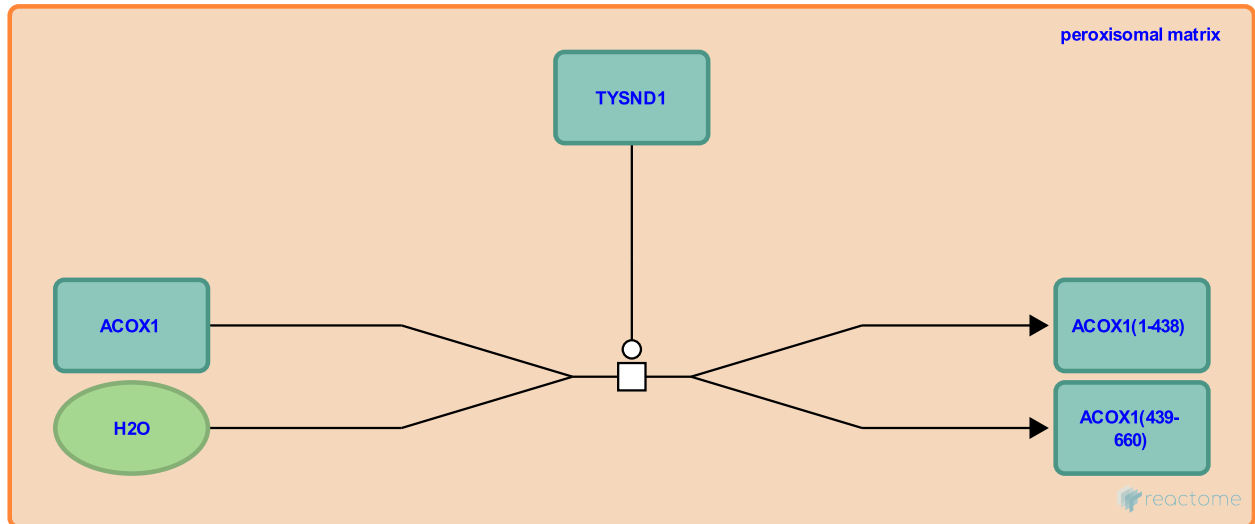
**Location:** [TYSND1 cleaves peroxisomal proteins](#)

**Stable identifier:** R-HSA-9033515

**Type:** transition

**Compartments:** peroxisomal matrix

**Inferred from:** [Tysnd1 cleaves Acox1 \(Mus musculus\)](#)



The trypsin-like serine-type endopeptidase TYSD1 cleaves ACOX1 between amino acid residues 438 and 439, yielding ACOX1(1-438) and ACOX1(439-660) (Okumoto et al. 2011, also inferred from mouse and rat homologs).

### Literature references

Kametani, Y., Okumoto, K., Fujiki, Y. (2011). Two proteases, trypsin domain-containing 1 (Tysnd1) and peroxisomal lon protease (PsLon), cooperatively regulate fatty acid  $\beta$ -oxidation in peroxisomal matrix. *J. Biol. Chem.*, 286, 44367-79. ↗

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2018-03-12	Reviewed	Azevedo, JE.

## TYSND1 cleaves AGPS ↗

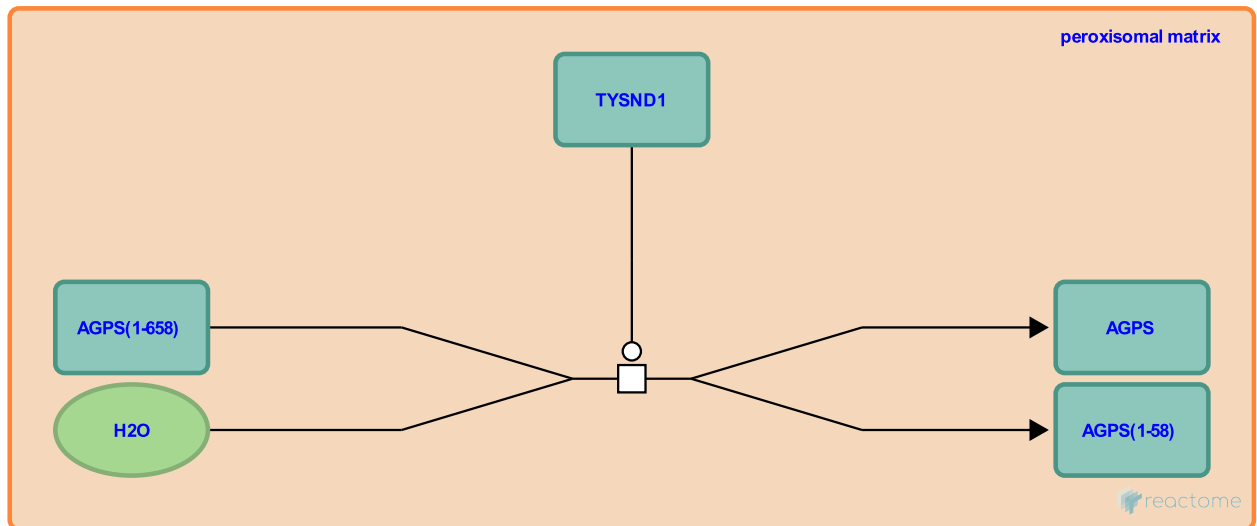
**Location:** [TYSND1 cleaves peroxisomal proteins](#)

**Stable identifier:** R-HSA-9033506

**Type:** transition

**Compartments:** peroxisomal matrix

**Inferred from:** [Tysnd1 cleaves Agps \(Mus musculus\)](#)



The trypsin-like serine-type endopeptidase TYSD1 cleaves AGPS between amino acid residues 58 and 59, yielding AGPS(1-58) and AGPS(59-658) (inferred from mouse homologs). In mice, knockout of TYSD1 causes reduced localization of AGPS to the peroxisome.

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## TYSND1 cleaves SCP2 ↗

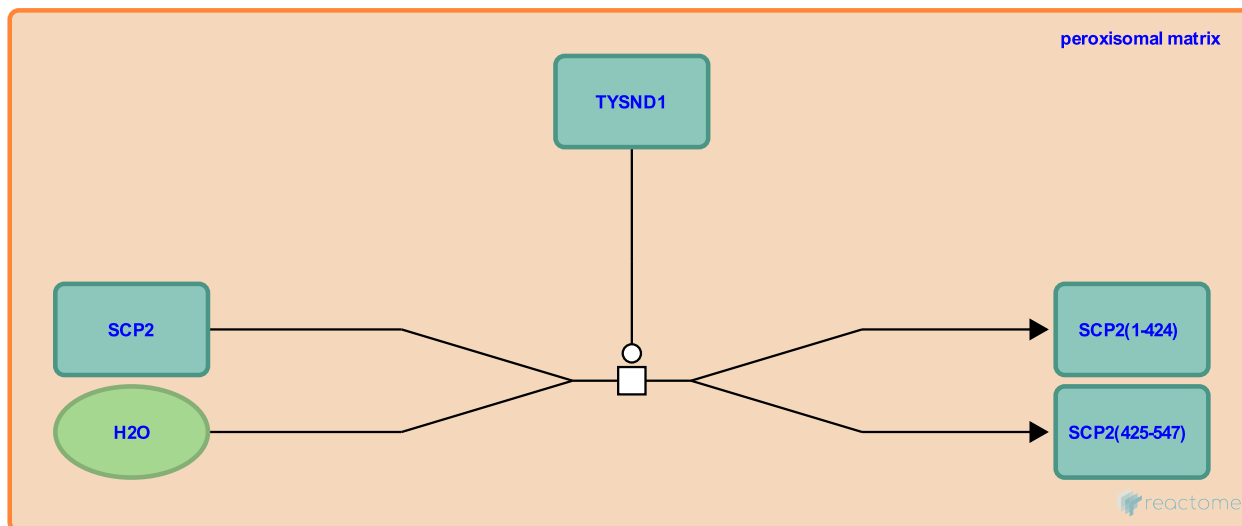
**Location:** [TYSND1 cleaves peroxisomal proteins](#)

**Stable identifier:** R-HSA-9033524

**Type:** transition

**Compartments:** peroxisomal matrix

**Inferred from:** [Tysnd1 cleaves Scp2 \(Mus musculus\)](#)



The trypsin-like serine-type endopeptidase TYSD1 cleaves SCP2 (also known as SCPX) between amino acid residues 424 and 425, yielding SCP2(1-424) and SCP2(425-547) (Okumoto et al. 2011, also inferred from mouse homologs).

### Literature references

Kametani, Y., Okumoto, K., Fujiki, Y. (2011). Two proteases, trypsin domain-containing 1 (Tysnd1) and peroxisomal lon protease (PsLon), cooperatively regulate fatty acid  $\beta$ -oxidation in peroxisomal matrix. *J. Biol. Chem.*, 286, 44367-79. ↗

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## TYSND1 cleaves PHYH ↗

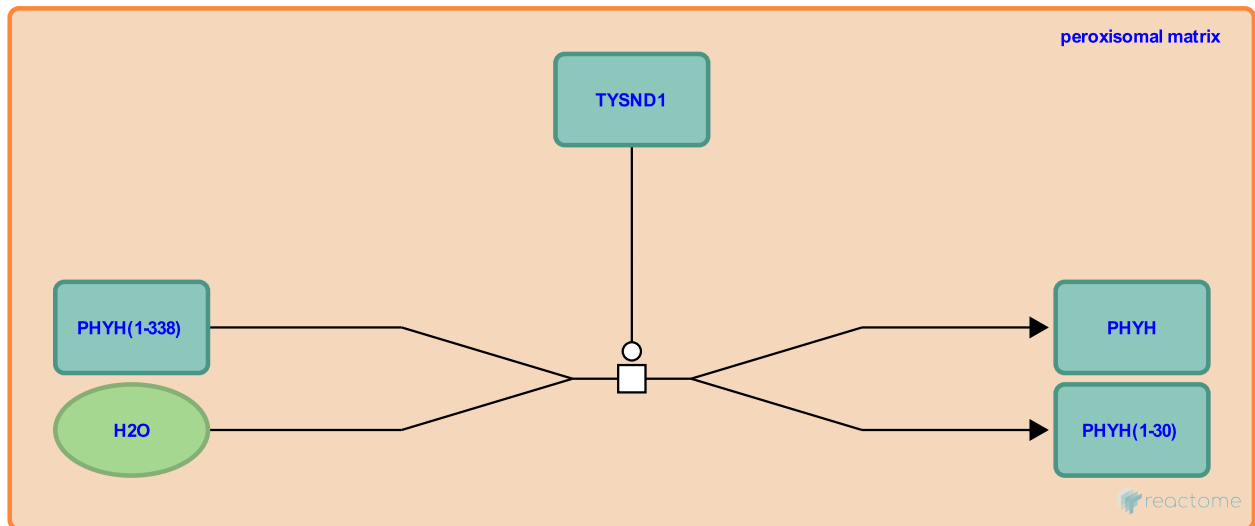
**Location:** [TYSND1 cleaves peroxisomal proteins](#)

**Stable identifier:** R-HSA-9033490

**Type:** transition

**Compartments:** peroxisomal matrix

**Inferred from:** [Tysnd1 cleaves Phyh \(Mus musculus\)](#)



The trypsin-like serine-type endopeptidase TYSND1 cleaves PHYH between amino acid residues 30 and 31, yielding PHYH(1-30) and PHYH(31-338). In mice, knockout of *Tysnd1* causes reduced localization of Phyh to peroxisomes.

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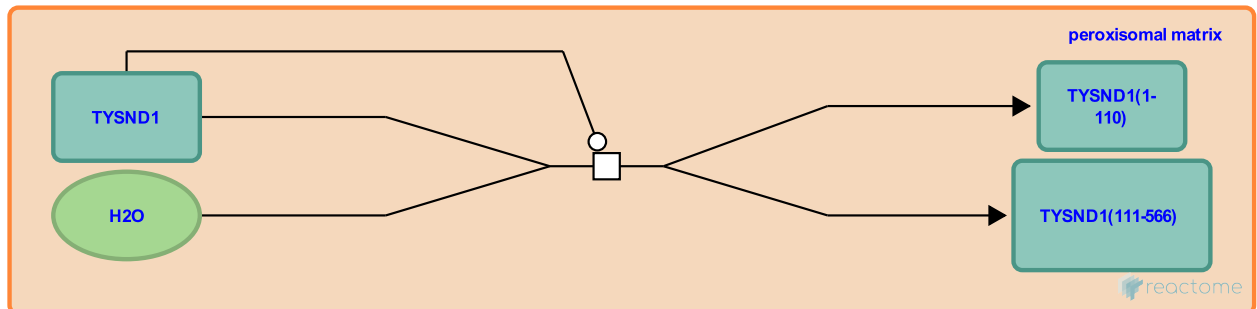
## TYSND1 cleaves YYSND1 ↗

**Location:** [TYSND1 cleaves peroxisomal proteins](#)

**Stable identifier:** R-HSA-9033520

**Type:** transition

**Compartments:** peroxisomal matrix



The trypsin-like serine-type endopeptidase YYSND1 cleaves YYSND1 between amino acid residues 110 and 111, yielding YYSND1(1-110) and YYSND1(111-566) (Okumoto et al. 2011). Self-cleavage of YYSND1 reduces its proteolytic activity.

### Literature references

Kametani, Y., Okumoto, K., Fujiki, Y. (2011). Two proteases, trypsin domain-containing 1 (Tysnd1) and peroxisomal lon protease (PsLon), cooperatively regulate fatty acid  $\beta$ -oxidation in peroxisomal matrix. *J. Biol. Chem.*, 286, 44367-79. ↗

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## TYSND1 cleaves HSD17B4 [↗](#)

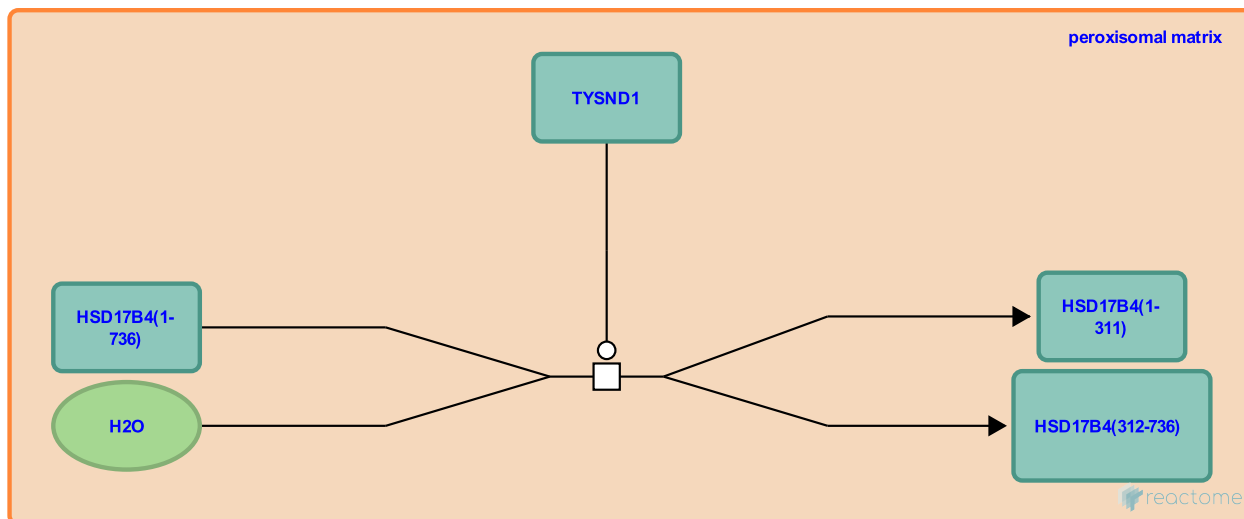
**Location:** [TYSND1 cleaves peroxisomal proteins](#)

**Stable identifier:** R-HSA-9033530

**Type:** transition

**Compartments:** peroxisomal matrix

**Inferred from:** [Tysnd1 cleaves Hsd17b4 \(Mus musculus\)](#)



The trypsin-like serine-type endopeptidase TYSD1 cleaves HSD17B4 (Peroxisomal multifunctional enzyme type 2, MFP-2) between amino acid residues 311 and 312, yielding HSD17B4(1-311) and HSD17B4(312-736) (Okumoto et al. 2011, also inferred from mouse homologs). HSD17B4(1-311) dehydrogenates 3-hydroxyacyl-CoA; HSD17B4(312-736) acts as an enoyl-CoA hydratase (Jiang et al. 1997, reviewed in Huyghe et al. 2006). (In vitro, HSD17B4(312-736) facilitates the transfer of 7-dehydrocholesterol and phosphatidylcholine between membranes.) The uncleaved protein (HSD17B4) also catalyzes these reactions.

### Literature references

Kametani, Y., Okumoto, K., Fujiki, Y. (2011). Two proteases, trypsin domain-containing 1 (Tysnd1) and peroxisomal lon protease (PsLon), cooperatively regulate fatty acid  $\beta$ -oxidation in peroxisomal matrix. *J. Biol. Chem.*, 286, 44367-79. [↗](#)

Souri, M., Hashimoto, T., Jiang, LL., Miyazawa, S. (1997). Structure of D-3-hydroxyacyl-CoA dehydratase/D-3-hydroxyacyl-CoA dehydrogenase bifunctional protein. *J Biochem*, 121, 364-9. [↗](#)

Baes, M., Van Veldhoven, PP., Huyghe, S., Mannaerts, GP. (2006). Peroxisomal multifunctional protein-2: the enzyme, the patients and the knockout mouse model. *Biochim Biophys Acta*, 1761, 973-94. [↗](#)

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