

SDS dimers:PXLP dehydrate L-Thr to 2AA

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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

- 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*

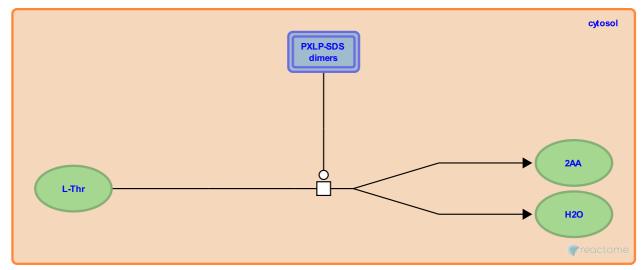
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Stable identifier: R-HSA-9014627

Type: transition

Compartments: cytosol



Various PXLP-dependent enzymes can catalyse α , β -elimination reactions of amino acid substrates, ultimately yielding α -keto (or 2-oxo-) acid products. However, these enzymes, such as L-serine dehydratase/L-threonine deaminase (SDS aka TDH), only form the enamine intermediate as the remainder of the reaction occurs in solution with the enamine intermediate tautomerising to the imine form, which then spontaneously hydrolyzes to the final α -keto acid product (Downs & Ernst 2015). SDS can dehydrate L-threonine (L-Thr) to form the intermediate enamine 2-aminoacrylate (2AA), which can damage the pyridoxal 5'-phosphate cofactor (PXLP) of various enzymes, causing inactivation and significant cellular damage if allowed to accumulate (Lambrecht et al. 2013). SDS exists as a homodimer and requires PXLP for activity (Sun et al. 2005). An isoform of SDS, serine dehydratase-like (SDSL aka SDH2), is found in human cancer cell lines and possesses lower catalytic activity than SDS (Yamada et al. 2008).

Literature references

- Bartlam, M., Rao, Z., Pang, H., Liu, Y., Sun, L. (2005). Crystal structure of the pyridoxal-5'-phosphate-dependent serine dehydratase from human liver. *Protein Sci.*, 14, 791-8. *¬*
- Yamada, T., Ogawa, H., Kasuya, T., Takata, Y., Komoto, J., Takusagawa, F. et al. (2008). A catalytic mechanism that explains a low catalytic activity of serine dehydratase like-1 from human cancer cells: crystal structure and sitedirected mutagenesis studies. *Biochim. Biophys. Acta, 1780,* 809-18. 7

Editions

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