ALAS condenses SUCC-CoA and Gly to form dALA

D'Eustachio, P., Jassal, B., Sassa, S.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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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. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

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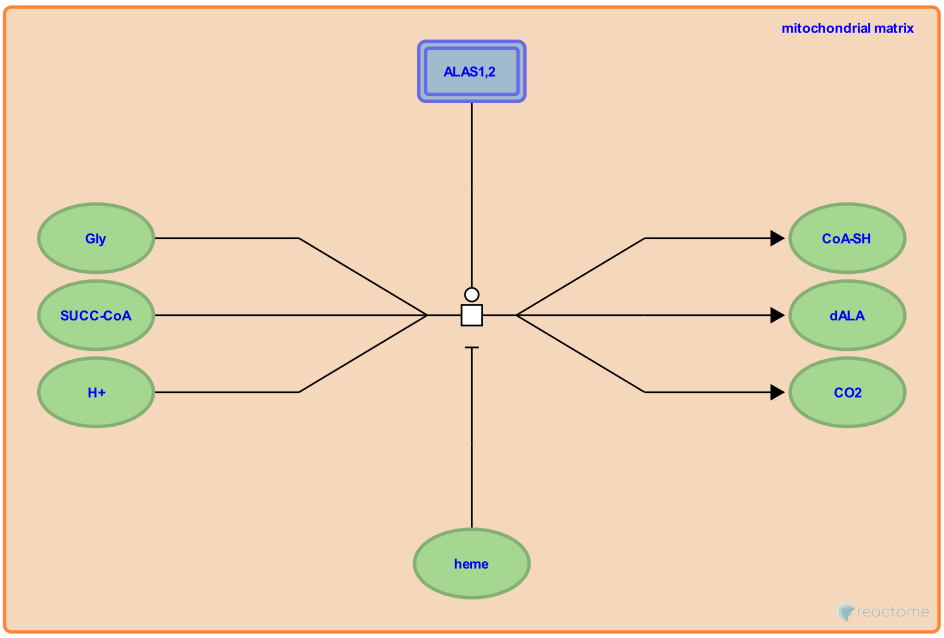
Stable identifier: R-HSA-189442

Type: transition

Compartments: mitochondrial matrix



The committed step for porphyrin synthesis is the formation of 5-aminolevulinate (ALA) by condensation of glycine (from the general amino acid pool) and succinyl-CoA (from the TCA cycle), in the mitochondrial matrix. The reaction is catalyzed by two different ALA synthases, one expressed ubiquitously (ALAS1) and the other only expressed in erythroid precursors (ALAS2). Both enzymes are expressed as homodimers and require pyridoxal 5-phosphate as a cofactor.
No disease-causing mutations of ALAS1 have been recognised in humans. Mutations in ALAS2 cause X-linked sideroblastic anaemia (XLSA), characterised by a microcytic hypochromic anaemia.

Literature references

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Heinz, DW., Jahn, D., Schubert, WD., van den Heuvel, J., Schulze, JO., Astner, I. (2005). Crystal structure of 5-aminolevulinate synthase, the first enzyme of heme biosynthesis, and its link to XLSA in humans. *EMBO J, 24*, 3166-77. ↗

Editions

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