Defective ABCD1 does not transfer LCFAs from cytosol to peroxisomal matrix

Jassal, B., Shukla, S.

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

26/04/2024

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. ↗

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. ↗

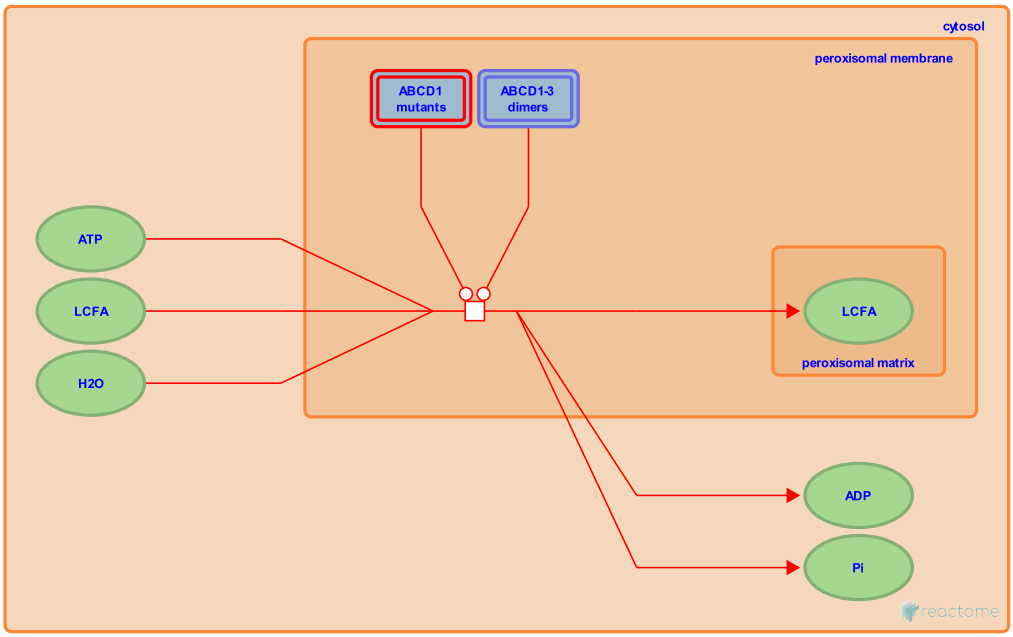
Defective ABCD1 does not transfer LCFAs from cytosol to peroxisomal matrix

Stable identifier: R-HSA-5684043

Type: transition

Compartments: peroxisomal membrane, cytosol

Diseases: adrenoleukodystrophy



The 70-kDa peroxisomal membrane protein (PMP70) and the adrenoleukodystrophy protein (ALDP aka ABCD1) are half ATP binding cassette (ABC) transporters in the peroxisome membrane. They are involved in metabolic transport of long and very long chain fatty acids into peroxisomes. Mutations in the ALD gene result in the X-linked neurodegenerative disorder adrenoleukodystrophy (ALD; MIM:300100). ABCD1 deficiency impairs the peroxisomal beta-oxidation of very long-chain fatty acids (VLCFA) and facilitates their further chain elongation by ELOVL1 resulting in accumulation of VLCFA in plasma and tissues. While all patients with ALD have mutations in the ABCD1 gene, there is no general genotype-phenotype correlation. Mutations causing ALD include R617C, S606L, M1V, G277R, R554H and W77_L82del (Krasemann et al. 1996, Fanen et al. 1994, Engelen et al. 2011, Coll et al. 2005, Park et al. 2014).

Literature references

Camps, C., Pàmpols, T., Girós, M., Coll, MJ., Palau, N., Ruiz, M. (2005). X-linked adrenoleukodystrophy in Spain. Identification of 26 novel mutations in the ABCD1 gene in 80 patients. Improvement of genetic counseling in 162 relative females. *Clin. Genet., 67*, 418-24.

Kim, HJ., Lee, PH., Kang, HC., Choi, BO., Park, HJ., Choi, YC. et al. (2014). Clinical and genetic aspects in twelve Korean patients with adrenomyeloneuropathy. *Yonsei Med. J., 55*, 676-82.

Guidoux, S., Goossens, M., Fanen, P., Sarde, CO., Mandel, JL., Aubourg, P. (1994). Identification of mutations in the putative ATP-binding domain of the adrenoleukodystrophy gene. *J. Clin. Invest., 94*, 516-20.

Koelman, JT., van Geel, BM., Sistermans, EA., de Visser, M., van der Kooi, AJ., Kemp, S. et al. (2011). X-linked adrenomyeloneuropathy due to a novel missense mutation in the ABCD1 start codon presenting as demyelinating neuropathy. *J. Peripher. Nerv. Syst., 16*, 353-5.

Korenke, GC., Hunneman, DH., Krasemann, EW., Meier, V., Hanefeld, F. (1996). Identification of mutations in the ALD-gene of 20 families with adrenoleukodystrophy/adrenomyeloneuropathy. *Hum. Genet., 97*, 194-7.

Editions

2015-03-18	Authored, Edited	Jassal, B.
2015-09-15	Reviewed	Shukla, S.