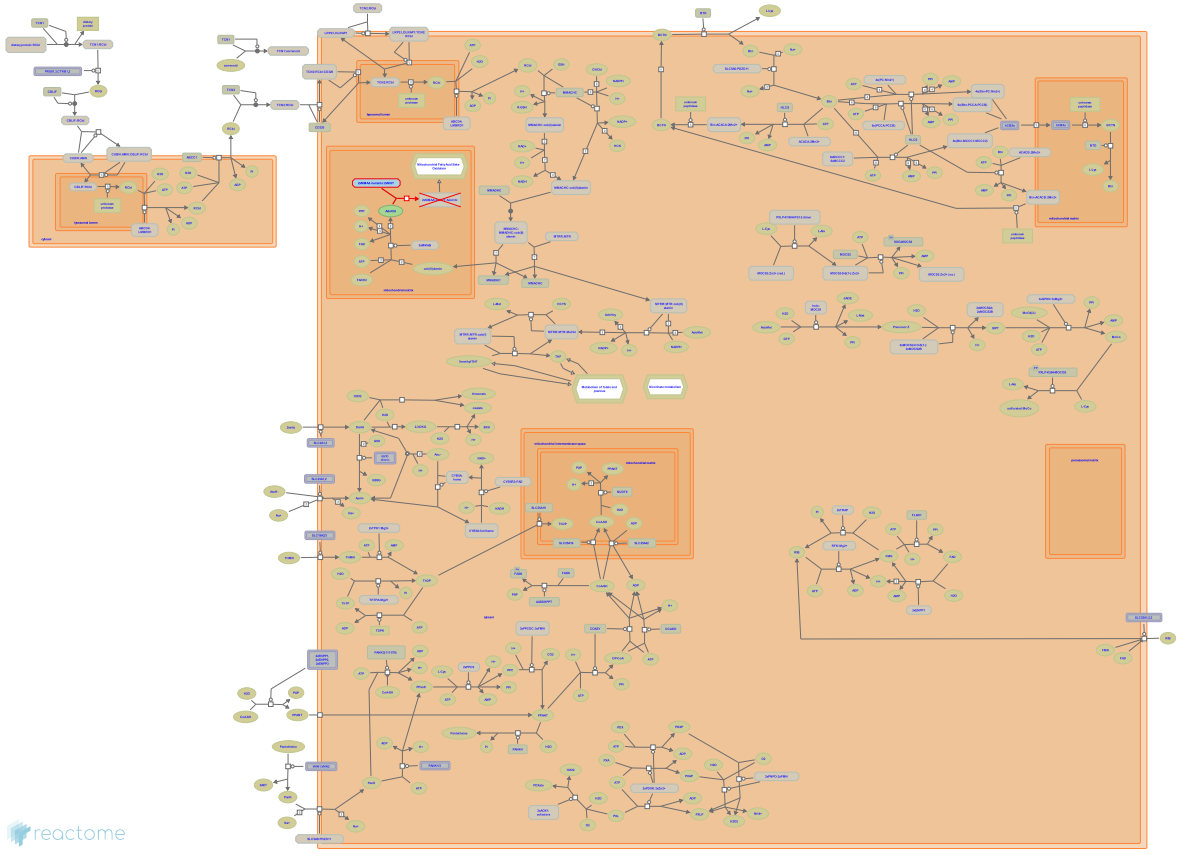
Defective MMAA causes MMA, cblA type



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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.

18/05/2024

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.

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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. ↗

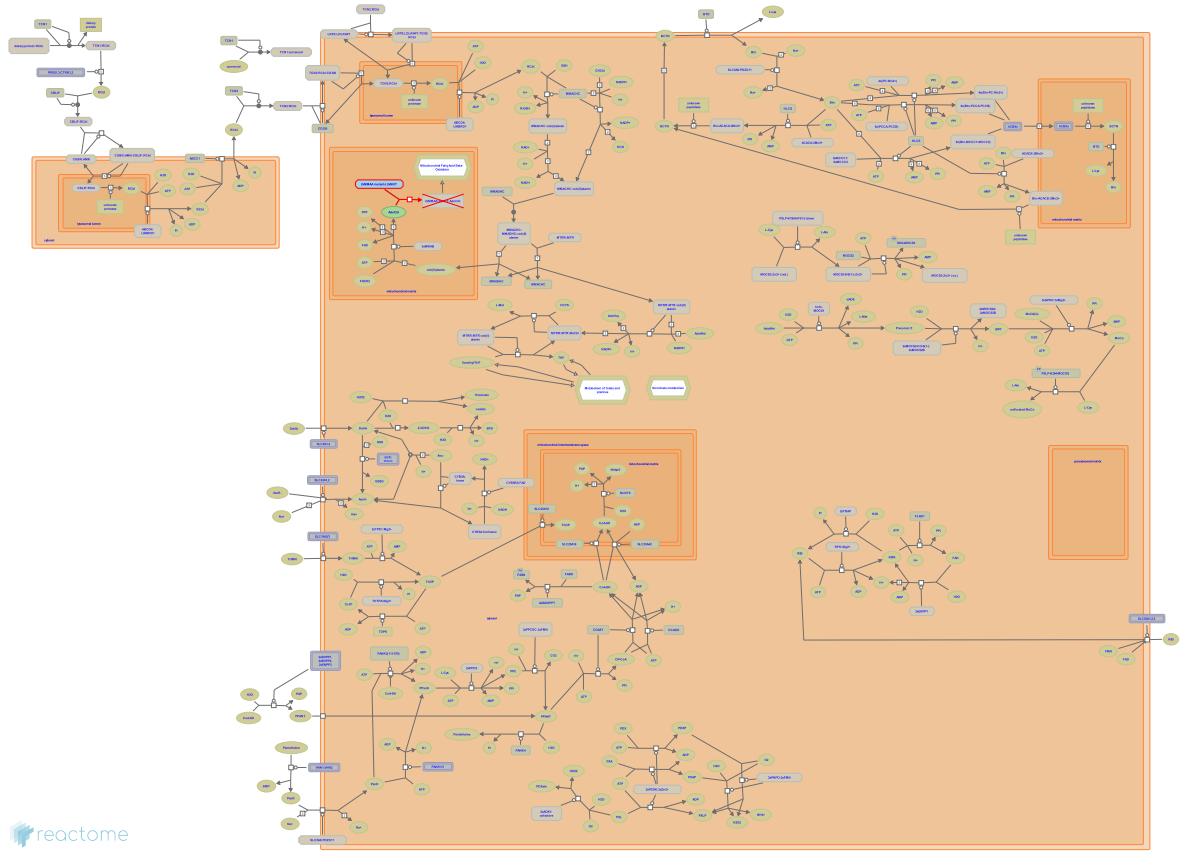
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

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. ↗

Defective MMAA causes MMA, cblA type ↗

Stable identifier: R-HSA-3359475

Diseases: methylmalonic acidemia



Defects in MMAA cause methylmalonic aciduria type cblA (cblA aka methylmalonic aciduria type A or vitamin B12-responsive methylmalonic aciduria of cblA complementation type; MIM:251100). Affected individuals accumulate methylmalonic acid in the blood and urine and are prone to potentially life threatening acidotic crises in infancy or early childhood (Dobson et al. 2002, Lerner-Ellis et al. 2004).

Literature references

Dobson, CM., Hudson, T., Doré, C., Gravel, RA., Rosenblatt, DS., Wu, X. et al. (2002). Identification of the gene responsible for the cblA complementation group of vitamin B12-responsive methylmalonic acidemia based on analysis of prokaryotic gene arrangements. *Proc. Natl. Acad. Sci. U.S.A., 99*, 15554-9. ↗

Dobson, CM., Doré, C., Gravel, RA., Rosenblatt, DS., Lepage, P., Leclerc, D. et al. (2004). Mutations in the MMAA gene in patients with the cblA disorder of vitamin B12 metabolism. *Hum. Mutat., 24*, 509-16. ↗

Editions

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2013-08-14	Reviewed	Watkins, D.

Defective MMAA does not protect MUT ↗

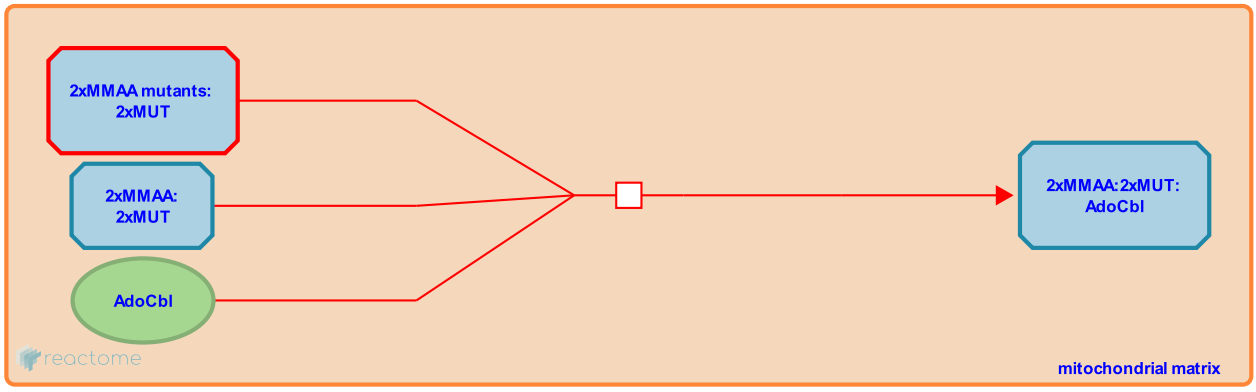
Location: Defective MMAA causes MMA, cblA type

Stable identifier: R-HSA-3322135

Type: transition

Compartments: mitochondrial matrix

Diseases: methylmalonic acidemia



Methylmalonic aciduria type A protein (MMAA) is thought to act as a chaperone to MUT, the enzyme which utilises adenosylcobalamin (AdoCbl) as a cofactor. MMAA is suggested to play a dual role with regards to MUT protection and reactivation. Some AdoCbl-dependent enzymes undergo suicide inactivation after catalysis due to the oxidative inactivation of Cbl. MMAA is thought to play a protective role to prevent MUT being inactivated in this way. Defects in MMAA cause methylmalonic aciduria type cblA (cblA aka methylmalonic aciduria type A or vitamin B12-responsive methylmalonicaciduria of cblA complementation type; MIM:251100). Affected individuals accumulate methylmalonic acid in the blood and urine and are prone to potentially life threatening acidotic crises in infancy or early childhood. Mutations causing cblA include MMAA Q95*, R145*, Y207C and D87Ifs*11 (Dobson et al. 2002, Lerner-Ellis et al. 2004).

Literature references

Flores, ME., García-Arellano, H., Takahashi-Íñiguez, T., Trujillo-Roldán, MA. (2011). Protection and reactivation of human methylmalonyl-CoA mutase by MMAA protein. *Biochem. Biophys. Res. Commun., 404*, 443-7. ↗

Froese, DS., Gravel, RA., Wu, X., Ugochukwu, E., Oppermann, U., Muniz, JR. et al. (2010). Structures of the human GTPase MMAA and vitamin B12-dependent methylmalonyl-CoA mutase and insight into their complex formation . *J. Biol. Chem., 285*, 38204-13. ↗

Dobson, CM., Hudson, T., Doré, C., Gravel, RA., Rosenblatt, DS., Wu, X. et al. (2002). Identification of the gene responsible for the cblA complementation group of vitamin B12-responsive methylmalonic acidemia based on analysis of prokaryotic gene arrangements. *Proc. Natl. Acad. Sci. U.S.A., 99*, 15554-9. ↗

Padovani, D., Banerjee, R. (2006). Assembly and protection of the radical enzyme, methylmalonyl-CoA mutase, by its chaperone. *Biochemistry, 45*, 9300-6. ↗

Niles, K., Worgan, LC., Rosenblatt, DS., Lepage, P., Hofmann, A., Kucic, T. et al. (2006). Spectrum of mutations in mut methylmalonic acidemia and identification of a common Hispanic mutation and haplotype. *Hum. Mutat., 27* , 31-43. ↗

Editions

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2013-08-14	Reviewed	Watkins, D.

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