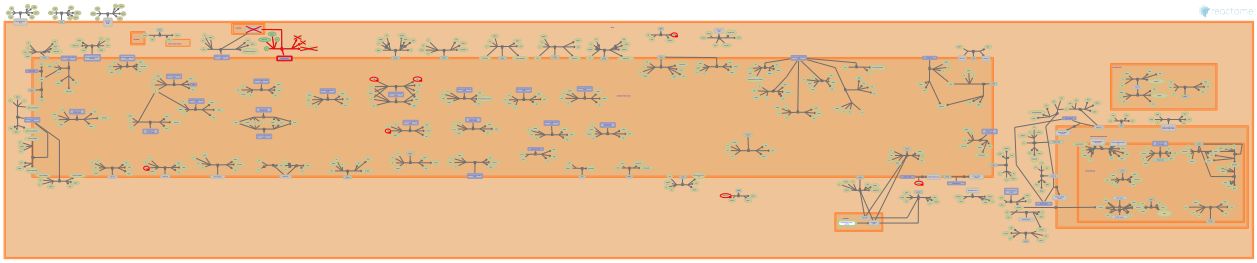
Defective CYP7B1 causes SPG5A and CBAS3



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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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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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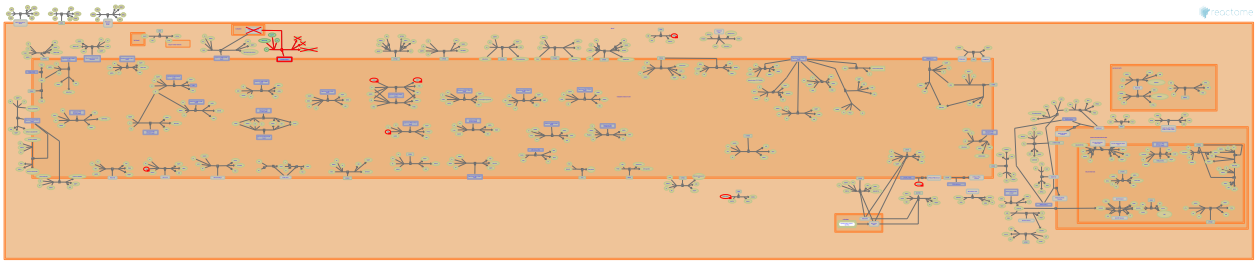
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Defective CYP7B1 causes SPG5A and CBAS3 ↗

Stable identifier: R-HSA-5579013

Diseases: hereditary spastic paraplegia



Bile acids are synthesised from cholesterol via two pathways - a classic neutral pathway involving cholesterol 7-alpha-hydroxylase (CYP7A1), and an acidic pathway involving 25-hydroxycholesterol 7-alpha-hydroxylase (CYP7B1). Defects in CYP7B1 can cause spastic paraplegia 5A (SPG5A), a neurodegenerative disorder characterised by a slow, gradual, progressive weakness and spasticity of the lower limbs (Tsaousidou et al. 2008). Defects in CYP7B1 can also cause Congenital bile acid synthesis defect 3 (CBAS3; MIM:613812), a disorder resulting in severe cholestasis, cirrhosis and liver synthetic failure. Hepatic CYP7B1 activity is undetectable (Setchell et al. 1998).

Literature references

Crosby, AH., Patel, H., Hentati, A., Lamont, PJ., Siddique, T., Simpson, MA. et al. (2008). Sequence alterations within CYP7B1 implicate defective cholesterol homeostasis in motor-neuron degeneration. *Am. J. Hum. Genet., 82*, 510-5 . ↗

Thompson, HR., Sokol, RJ., Lathe, R., Russell, DW., Setchell, KD., Weslie Tyson, R. et al. (1998). Identification of a new inborn error in bile acid synthesis: mutation of the oxysterol 7alpha-hydroxylase gene causes severe neonatal liver disease. *J Clin Invest, 102*, 1690-703. ↗

Editions

2014-06-06	Authored, Edited	Jassal, B.
2014-11-03	Reviewed	Nakaki, T.

Defective CYP7B1 does not 7-hydroxylate 25OH-CHOL ↗

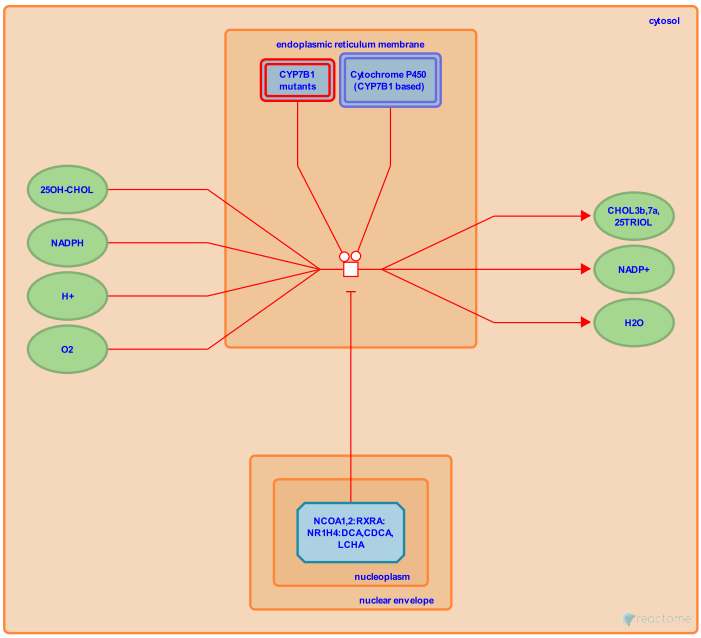
Location: Defective CYP7B1 causes SPG5A and CBAS3

Stable identifier: R-HSA-5602885

Type: transition

Compartments: endoplasmic reticulum membrane, cytosol

Diseases: hereditary spastic paraplegia



25-hydroxycholesterol 7-alpha-hydroxylase (CYP7B1) normally 7alpha-hydroxylates 25-hydroxycholesterol (25OH-CHOL) to cholest-5-ene-3beta,7alpha,25-triol (CHOL3b,7a,25TRIOL). Defects in CYP7B1 can cause spastic paraplegia 5A, autosomal recessive (SPG5A; MIM:270800), a neurodegenerative disorder characterised by a slow, gradual, progressive weakness and spasticity of the lower limbs (Tsaousidou et al. 2008). Mutations causing SPG5A include S363F, G57R, R417H, F216S, Y275*, F470I, G87V and T297A (Tsaousidou et al. 2008, Schule et al. 2009, Goizet et al. 2009, Arnoldi et al. 2012). Defects in CYP7B1 can also cause congenital bile acid synthesis defect 3 (CBAS3; MIM:613812), a disorder resulting in severe cholestasis, cirrhosis and liver synthetic failure. Hepatic CYP7B1 activity is undetectable (Setchell et al. 1998). A mutation causing CBAS3 is R388* (Setchell et al. 1998).

Literature references

Crosby, AH., Patel, H., Hentati, A., Lamont, PJ., Siddique, T., Simpson, MA. et al. (2008). Sequence alterations within CYP7B1 implicate defective cholesterol homeostasis in motor-neuron degeneration. *Am. J. Hum. Genet., 82*, 510-5 . ↗

Thompson, HR., Sokol, RJ., Lathe, R., Russell, DW., Setchell, KD., Weslie Tyson, R. et al. (1998). Identification of a new inborn error in bile acid synthesis: mutation of the oxysterol 7alpha-hydroxylase gene causes severe neonatal liver disease. *J Clin Invest, 102*, 1690-703. ↗

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Editions

2014-06-25	Authored, Edited	Jassal, B.
2014-11-03	Reviewed	Nakaki, T.

Table of Contents