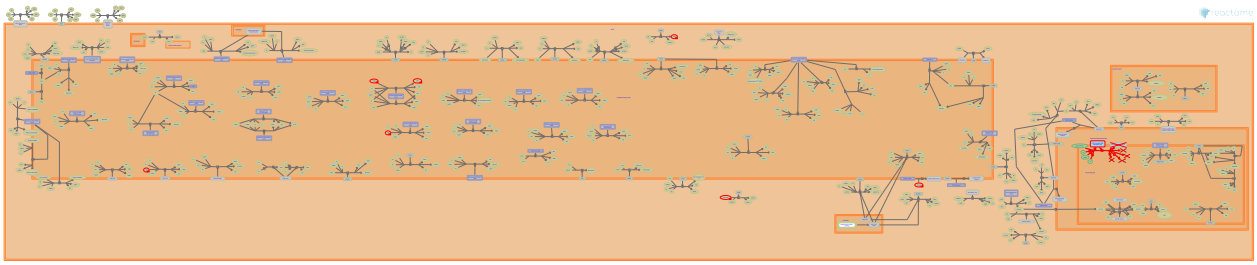
Defective CYP11A1 causes AICSR



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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

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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. ↗

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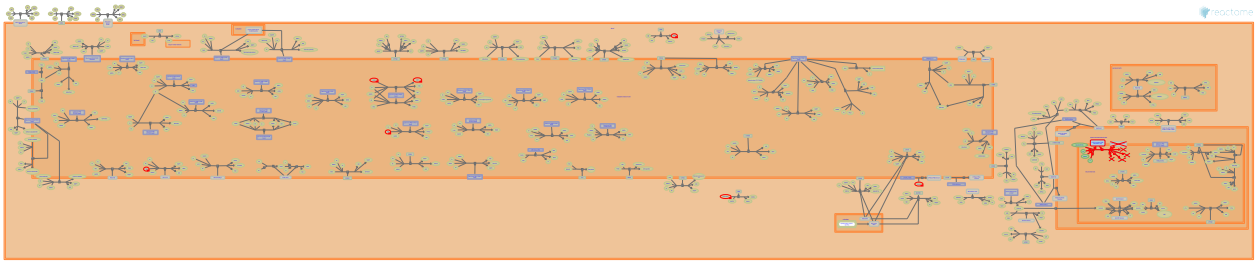
Defective CYP11A1 causes AICSR ↗

Stable identifier: R-HSA-5579026

Diseases: congenital adrenal insufficiency



Cholesterol side-chain cleavage enzyme, mitochondrial (CYP11A1) normally catalyses the side-chain cleavage of cholesterol to form pregnenolone. Defects in CYP11A1 can cause Adrenal insufficiency, congenital, with 46,XY sex reversal (AICSR; MIM:613743). This is a rare disorder that can present as acute adrenal insufficiency in infancy with elevated ACTH and plasma renin activity and low or absent adrenal steroids. The severest phenotype is loss-of-function mutations associated with prematurity, complete under-androgenisation and severe, early-onset adrenal failure (Kim et al. 2008).

Literature references

Huang, N., Achermann, JC., Quigley, CA., Miller, WL., AvRuskin, TW., Lin, L. et al. (2008). Severe combined adrenal and gonadal deficiency caused by novel mutations in the cholesterol side chain cleavage enzyme, P450scc. *J. Clin. Endocrinol. Metab., 93*, 696-702. ↗

Editions

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

Defective CYP11A1 does not cleave 20a,22b-DHCHOL ↗

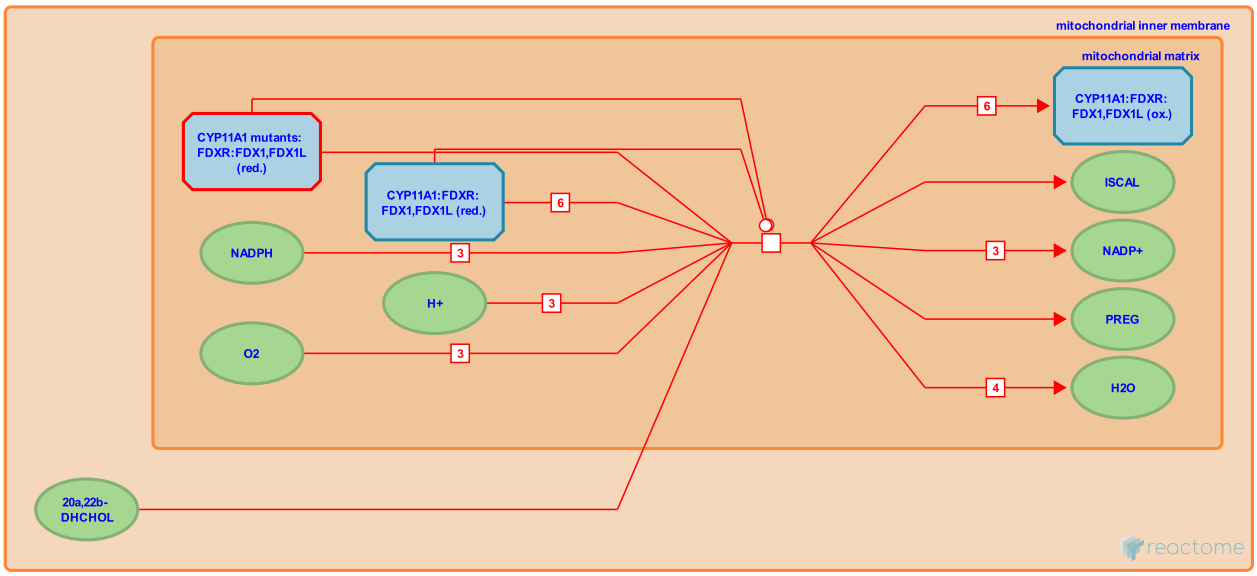
Location: Defective CYP11A1 causes AICSR

Stable identifier: R-HSA-5580269

Type: transition

Compartments: mitochondrial matrix

Diseases: congenital adrenal insufficiency



Cholesterol side-chain cleavage enzyme, mitochondrial (CYP11A1) normally catalyses the side-chain cleavage of cholesterol to form pregnenolone. CYP11A1 is the active unit of a complex comprising adrenodoxin reductase (FDXR), adrenodoxin (FDX, or adrenodoxin-like protein FDX1L) (Strushkevich et al. 2011). Defects in CYP11A1 can cause Adrenal insufficiency, congenital, with 46,XY sex reversal (AICSR; MIM:613743). This is a rare disorder that can present as acute adrenal insufficiency in infancy with elevated ACTH and plasma renin activity and low or absent adrenal steroids. Although milder forms can present, associated with partial loss of enzyme activity, the severest phenotype is associated with prematurity, complete underandrogenisation and severe, early-onset adrenal failure. CYP11A1 mutations causing complete loss of function are a 6bp insertion resulting in the insertion of glycine and aspartate codons, a 1bp deletion resulting in a premature stop at 288 and the missense mutation V415E (Tajima et al. 2001, Hiort et al. 2005, Kim et al. 2008, Sahakitrungruang et al. 2010).

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Park, HW., Grabovec, I., Usanov, S., MacKenzie, F., Cherkesova, T., Strushkevich, N. (2011). Structural basis for pregnenolone biosynthesis by the mitochondrial monooxygenase system. *Proc. Natl. Acad. Sci. U.S.A., 108*, 10139-43. ↗

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Miller, WL., Nakae, J., Tajima, T., Kouda, N., Fujieda, K. (2001). Heterozygous mutation in the cholesterol side chain cleavage enzyme (p450scc) gene in a patient with 46,XY sex reversal and adrenal insufficiency. *J. Clin. Endocrinol. Metab., 86*, 3820-5. ↗

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Editions

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

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