

AKR1D1 gene

aldo-keto reductase family 1 member D1

Normal Function

The *AKR1D1* gene provides instructions for making an enzyme called 3-oxo-5-beta(β)-steroid 4-dehydrogenase. This enzyme is found in liver cells. It participates in the production of bile acids, which are a component of a digestive fluid called bile. Bile acids stimulate bile flow and helps absorb fats and fat-soluble vitamins. Bile acids are produced from cholesterol in a multi-step process. The 3-oxo-5- β -steroid 4-dehydrogenase enzyme is responsible for the third step in that process, which converts 7alpha(α)-hydroxy-4-cholesten-3-one to 7 α -hydroxy-5 β -cholesten-3-one.

Health Conditions Related to Genetic Changes

Congenital bile acid synthesis defect type 2

More than 10 mutations in the AKR1D1 gene have been found to cause congenital bile acid synthesis defect type 2. This condition is characterized by cholestasis, a condition that impairs the production and release of a digestive fluid called bile from liver cells. Most of the AKR1D1 gene mutations replace single protein building blocks (amino acids) in the enzyme. These mutations result in production of a 3-oxo-5- β -steroid 4-dehydrogenase enzyme with severely reduced function. Without enough functional enzyme, the conversion of 7α -hydroxy-4-cholesten-3-one to 7α -hydroxy-5 β -cholesten-3-one is impaired. The 7α -hydroxy-4-cholesten-3-one instead gets converted into abnormal bile acid compounds that cannot be transported out of the liver into the intestine, where the bile acids are needed to digest fats. This impaired production and release of bile acids leads to cholestasis. As a result, cholesterol and abnormal bile acids build up in the liver and fat-soluble vitamins are not absorbed, leading to the signs and symptoms of congenital bile acid synthesis defect type 2.

Other Names for This Gene

- 3-oxo-5-beta-steroid 4-dehydrogenase
- 3o5bred
- 5-beta-reductase
- AK1D1 HUMAN
- aldo-keto reductase family 1, member D1

- delta 4-3-ketosteroid-5-beta-reductase
- delta(4)-3-ketosteroid 5-beta-reductase
- delta(4)-3-oxosteroid 5-beta-reductase
- SRD5B1
- steroid 5-beta-reductase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

Tests of AKR1D1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6718[geneid])

Scientific Articles on PubMed

PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28AKR1D1%5BTIAB%5D%29+OR+%28%28delta-4-3-ketosteroid-5-beta-reductase%5BTIAB%5D%29+OR+%285-beta-reductase%5BTIAB%5D%29+OR+%28steroid+5-beta-reductase%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

ALDO-KETO REDUCTASE FAMILY 1, MEMBER D1; AKR1D1 (https://omim.org/entry/604741)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6718)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=AKR1D1[gene])

References

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- Jin Y, Chen M, Penning TM. Rate of steroid double-bond reduction catalysed bythe human steroid 5beta-reductase (AKR1D1) is sensitive to steroid structure: implications for steroid metabolism and bile acid synthesis. Biochem J. 2014 Aug15; 462(1):163-71. doi: 10.1042/BJ20140220. Citation on PubMed (https://pubmed.ncbi. nlm.nih.gov/24894951) or Free article on PubMed Central (https://www.ncbi.nlm.nih.

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- Lemonde HA, Custard EJ, Bouquet J, Duran M, Overmars H, Scambler PJ, ClaytonPT. Mutations in SRD5B1 (AKR1D1), the gene encoding delta(4)-3oxosteroid5beta-reductase, in hepatitis and liver failure in infancy. Gut. 2003Oct;52(10):1494-9. doi: 10.1136/gut.52.10.1494. Citation on PubMed (https://pubmed.ncbi.n lm.nih.gov/12970144) or Free article on PubMed Central (https://www.ncbi.nlm.nih.g ov/pmc/articles/PMC1773813/)
- Mindnich R, Drury JE, Penning TM. The effect of disease associated pointmutations on 5beta-reductase (AKR1D1) enzyme function. Chem Biol Interact. 2011 May30; 191(1-3):250-4. doi: 10.1016/j.cbi.2010.12.020. Epub 2010 Dec 24. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21185810) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3101292/)

Genomic Location

The *AKR1D1* gene is found on chromosome 7 (https://medlineplus.gov/genetics/chromosome/7/).

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