HSD17B4 gene

hydroxysteroid 17-beta dehydrogenase 4

Normal Function

The *HSD17B4* gene provides instructions for making the D-bifunctional protein. This protein is an enzyme, which means that it helps specific biochemical reactions take place. D-bifunctional protein is so named because it aids in two biochemical reactions.

The D-bifunctional protein is found in sac-like cell structures (organelles) called peroxisomes, which contain a variety of enzymes that break down many different substances. The D-bifunctional protein is involved in the breakdown of certain molecules called fatty acids. The protein has two separate regions (domains) with enzyme activity, called the hydratase and dehydrogenase domains. These domains help carry out the second and third steps, respectively, of a process called the peroxisomal fatty acid beta-oxidation pathway. This process shortens the fatty acid molecules by two carbon atoms at a time until the fatty acids are converted to a molecule called acetyl-CoA, which is transported out of the peroxisomes for reuse by the cell.

Health Conditions Related to Genetic Changes

D-bifunctional protein deficiency

More than 60 *HSD17B4* gene mutations have been identified in individuals with D-bifunctional protein deficiency, a severe disorder that causes deterioration of nervous system functions (neurodegeneration) beginning in infancy. *HSD17B4* gene mutations that cause D-bifunctional protein deficiency can affect one or both of the enzymatic activities of D-bifunctional protein; however, this distinction does not seem to affect the severity or features of the disorder.

Impairment of one or both of the D-bifunctional protein's enzymatic activities prevents it from breaking down fatty acids efficiently. As a result, these fatty acids accumulate in the body. It is unclear how fatty acid accumulation leads to the specific features of D-bifunctional protein deficiency; however, the accumulation may result in abnormal development of the brain and the breakdown of myelin, which is the covering that protects nerves and promotes the efficient transmission of nerve impulses. Destruction of myelin leads to a loss of myelin-containing tissue (white matter) in the brain and spinal cord; loss of white matter is described as leukodystrophy. Abnormal brain

development and leukodystrophy likely underlie the neurological abnormalities that occur in D-bifunctional protein deficiency.

Perrault syndrome

At least two *HSD17B4* gene mutations have been found to cause Perrault syndrome, a condition characterized by hearing loss in affected males and females and ovarian abnormalities in affected females. The *HSD17B4* gene mutations involved in this condition reduce the amount of functional D-bifunctional protein that is produced. It is not known what effect these mutations have on fatty acid breakdown in affected individuals or how the mutations lead to the signs and symptoms of Perrault syndrome.

Other Names for This Gene

- 17-beta-HSD 4
- 17-beta-HSD IV
- 17-beta-hydroxysteroid dehydrogenase 4
- 17beta-estradiol dehydrogenase type IV
- 3-alpha,7-alpha,12-alpha-trihydroxy-5-beta-cholest-24-enoyl-CoA hydratase
- beta-hydroxyacyl dehydrogenase
- beta-keto-reductase
- D-3-hydroxyacyl-CoA dehydratase
- D-bifunctional protein, peroxisomal
- DBP
- hydroxysteroid (17-beta) dehydrogenase 4
- MFE-2
- MPF-2
- multifunctional protein 2
- peroxisomal multifunctional enzyme type 2
- peroxisomal multifunctional protein 2
- PRLTS1
- SDR8C1
- short chain dehydrogenase/reductase family 8C, member 1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of HSD17B4 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3295[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28HSD17B4%5BTIAB%5D%29+OR+%28%2817-beta-HSD+IV%5BTIAB%5D%29+OR+%2817-beta-hydroxysteroid+dehydrogenase+4%5BTIAB%5D%29+OR+%28beta-hydroxyacyl+dehydrogenase%5BTIAB%5D%29+OR+%28beta-keto-reductase%5BTIAB%5D%29+OR+%28D-3-hydroxyacyl-CoA+dehydratase%5BTIAB%5D%29+OR+%28MFE-2%5BTIAB%5D%29+OR+%28MPF-2%5BTIAB%5D%29+OR+%28peroxisomal+multifunctional+enzyme+type+2%5BTIAB%5D%29+OR+%28peroxisomal+multifunctional+protein+2%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

- 17-BETA-HYDROXYSTEROID DEHYDROGENASE IV; HSD17B4 (https://omim.org/entry/601860)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3295)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=HSD17B4[gene])

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Genomic Location

The *HSD17B4* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

Last updated December 1, 2014