FA2H gene

fatty acid 2-hydroxylase

Normal Function

The *FA2H* gene provides instructions for making an enzyme called fatty acid 2-hydroxylase. This enzyme modifies fatty acids, which are building blocks used to make fats (lipids). Specifically, fatty acid 2-hydroxylase adds a single oxygen atom to a hydrogen atom at a particular point on a fatty acid to create a 2-hydroxylated fatty acid. Certain 2-hydroxylated fatty acids are important in forming normal myelin; myelin is the protective covering that insulates nerves and ensures the rapid transmission of nerve impulses. The part of the brain and spinal cord that contains myelin is called white matter.

Health Conditions Related to Genetic Changes

Fatty acid hydroxylase-associated neurodegeneration

At least nine mutations in the *FA2H* gene have been identified in people with fatty acid hydroxylase-associated neurodegeneration (FAHN). FAHN is a progressive disorder of the nervous system characterized by problems with movement and vision that begin during childhood or adolescence and worsen with age. Brain scans of affected individuals show abnormal accumulation of iron in the brain, especially in a region that is involved in movement.

The *FA2H* gene mutations that cause FAHN reduce or eliminate the function of the fatty acid 2-hydroxylase enzyme. Reduction of this enzyme's function may result in abnormal myelin that is prone to deterioration (demyelination), leading to a loss of white matter (leukodystrophy). Leukodystrophy is likely involved in the development of the movement problems and other neurological abnormalities that occur in FAHN. Iron accumulation in the brain is probably also involved, although it is unclear how *FA2H* gene mutations lead to the buildup of iron.

People with *FA2H* gene mutations and some of the movement problems seen in FAHN were once classified as having a separate disorder called spastic paraplegia 35. People with mutations in this gene resulting in intellectual decline and optic nerve atrophy were said to have a disorder called *FA2H*-related leukodystrophy. However, these conditions are now generally considered to be forms of FAHN.

Other Names for This Gene

- FA2H_HUMAN
- FAAH
- FAH1
- fatty acid alpha-hydroxylase
- fatty acid hydroxylase domain containing 1
- FAXDC1
- FLJ25287
- SCS7
- spastic paraplegia 35 (autosomal recessive)
- SPG35

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of FA2H (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=79152[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28FA2H%5BTIAB%5D%29+OR+%28fatty+acid+2-hydroxylase%5BTIAB%5D%29%29+OR+%28%28FAH1%5BTIAB%5D%29+OR+%28SCS7%5BTIAB%5D%29+OR+%28SPG35%5BTIAB%5D%29+OR+%28fatty+acid+alpha-hydroxylase%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+AND+%22last+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- FATTY ACID 2-HYDROXYLASE; FA2H (https://omim.org/entry/611026)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/79152)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=FA2H[gene])

References

- Alderson NL, Rembiesa BM, Walla MD, Bielawska A, Bielawski J, Hama H.

Thehuman FA2H gene encodes a fatty acid 2-hydroxylase. J Biol Chem. 2004 Nov19;279(47) :48562-8. doi: 10.1074/jbc.M406649200. Epub 2004 Aug 27. Citation on PubMed (ht tps://pubmed.ncbi.nlm.nih.gov/15337768)

- Dick KJ, Eckhardt M, Paisan-Ruiz C, Alshehhi AA, Proukakis C, Sibtain NA,Maier H, Sharifi R, Patton MA, Bashir W, Koul R, Raeburn S, Gieselmann V, HouldenH, Crosby AH. Mutation of FA2H underlies a complicated form of hereditary spasticparaplegia (SPG35). Hum Mutat. 2010 Apr;31(4):E1251-60. doi: 10.1002/ humu.21205. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20104589)
- Edvardson S, Hama H, Shaag A, Gomori JM, Berger I, Soffer D, Korman SH, Taustein I, Saada A, Elpeleg O. Mutations in the fatty acid 2-hydroxylase geneare associated with leukodystrophy with spastic paraparesis and dystonia. Am JHum Genet. 2008 Nov;83(5):643-8. doi: 10.1016/j.ajhg.2008.10.010. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19068277) or Free article on PubMed Central (http s://www.ncbi.nlm.nih.gov/pmc/articles/PMC2668027/)
- Gregory A, Hayflick SJ. Genetics of neurodegeneration with brain ironaccumulation. Curr Neurol Neurosci Rep. 2011 Jun;11(3):254-61. doi:10.1007/s11910-011-0181-3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21286947)
- Gregory A, Venkateswaran S, Hayflick SJ. Fatty Acid Hydroxylase-AssociatedNeurodegeneration. 2011 Jun 28 [updated 2018 Sep 27]. In: Adam MP, Feldman J,Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors.GeneReviews(R) [Internet]. Seattle (WA): University of Washington,Seattle; 1993-2024. Available from http://www.ncbi.nlm.nih.gov/books/NBK56080/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21735565)
- Kruer MC, Paisan-Ruiz C, Boddaert N, Yoon MY, Hama H, Gregory A, Malandrini A, Woltjer RL, Munnich A, Gobin S, Polster BJ, Palmeri S, Edvardson S, Hardy J, Houlden H, Hayflick SJ. Defective FA2H leads to a novel form of neurodegenerationwith brain iron accumulation (NBIA). Ann Neurol. 2010 Nov;68(5): 611-8. doi:10.1002/ana.22122. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov /20853438)
- Schneider SA, Bhatia KP. Three faces of the same gene: FA2H linksneurodegeneration with brain iron accumulation, leukodystrophies, and hereditaryspastic paraplegias. Ann Neurol. 2010 Nov;68(5):575-7. doi: 10.1002/ana. 22211. Noabstract available. Erratum In: Ann Neurol. 2011 Jul;70(1):187. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21031573)

Genomic Location

The *FA2H* gene is found on chromosome 16 (https://medlineplus.gov/genetics/chromos ome/16/).

Last updated October 1, 2012