FAH gene

fumarylacetoacetate hydrolase

Normal Function

The *FAH* gene provides instructions for making an enzyme called fumarylacetoacetate hydrolase. This enzyme is abundant in the liver and kidneys, and smaller amounts are found in many tissues throughout the body. Fumarylacetoacetate hydrolase is the last in a series of five enzymes that work to break down the amino acid tyrosine, a protein building block found in many foods. Specifically, fumarylacetoacetate hydrolase converts a tyrosine byproduct called fumarylacetoacetate into smaller molecules that are either excreted by the kidneys or used to produce energy or make other substances in the body.

Health Conditions Related to Genetic Changes

Tyrosinemia

At least 86 *FAH* mutations have been found that cause tyrosinemia type I. This condition is characterized by severe liver and kidney disease, neurological problems, and other signs and symptoms that begin in infancy. The altered *FAH* gene that causes this condition produces an unstable or inactive enzyme, which results in reduced or absent fumarylacetoacetate hydrolase activity. The most common *FAH* mutation disrupts the way the gene's instructions are used to make the enzyme. This mutation (written IVS12 + 5G>A) is called a splice-site mutation and results in an abnormally short enzyme. Without sufficient fumarylacetoacetate hydrolase activity, tyrosine and its byproducts are not properly broken down. As a result, fumarylacetoacetate accumulates in the liver and kidneys. Elevated levels of fumarylacetoacetate are thought to be toxic to cells and accumulation of this substance likely causes the liver and kidney problems and other features that are characteristic of tyrosinemia type I.

In several cases of tyrosinemia type I, the *FAH* gene mutation has been observed to revert to the normal state in some liver cells. If enough cells have the reverted gene, which produces normal fumarylacetoacetate hydrolase, some level of enzyme activity is achieved. Researchers have found a correlation between the severity of symptoms and the extent of reversion in liver cells. People with severe symptoms of tyrosinemia type I have few reverted cells, while those with milder symptoms have many cells with the reverted *FAH* gene.

Other Names for This Gene

- beta-diketonase
- FAA
- FAAA_HUMAN
- fumarylacetoacetase
- fumarylacetoacetate hydrolase (fumarylacetoacetase)

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of FAH (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2184[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28FAH%5BTIAB%5D%29+OR+%28fumarylacetoacetate+hydrolase%5BTIAB%5D%29%29+OR+%28fumarylacetoacetase%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2520+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- FUMARYLACETOACETATE HYDROLASE; FAH (https://omim.org/entry/613871)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/2184)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=FAH[gene])

References

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Genomic Location

The *FAH* gene is found on chromosome 15 (https://medlineplus.gov/genetics/chromosome/15/).

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