HGD gene

homogentisate 1,2-dioxygenase

Normal Function

The *HGD* gene provides instructions for making an enzyme called homogentisate 1,2-dioxygenase, which is active mainly in the liver and kidneys. This enzyme participates in a multi step process that breaks down two protein building blocks (amino acids), phenylalanine and tyrosine. They get broken down when they are no longer needed or when there are too many of them. These two amino acids also play a role in making certain brain chemicals (neurotransmitters), hormones, and pigments.

Homogentisate 1,2-dioxygenase is responsible for a specific step in the breakdown of phenylalanine and tyrosine. Previous steps convert the two amino acids into a molecule called homogentisic acid. Homogentisate 1,2-dioxygenase adds two oxygen atoms to homogentisic acid, converting it to another molecule called maleylacetoacetate. Other enzymes break down maleylacetoacetate into smaller molecules that are later used for energy or to make other products that can be used by the body.

Health Conditions Related to Genetic Changes

Alkaptonuria

Hundreds of variants (also called mutations) in the *HGD* gene have been found to cause alkaptonuria. This condition is characterized by arthritis,kidney stones, areas of dark pigmentation, and dark urine. Most of the HGD gene variants change single amino acids in the homogentisate 1,2-dioxygenase enzyme. These changes severely reduce the function of the homogentisate 1,2-dioxygenase enzyme.

Without a fully functional version of this enzyme, phenylalanine and tyrosine are not broken down properly, and homogentisic acid builds up in the body. Excess homogentisic acid settles in connective tissues and forms a substance called ochronotic pigment, which causes cartilage and skin to darken. Over time, this pigment can build up and harden (calcify), leading to health problems in people with alkaptonuria. Excess homogentisic acid is also excreted in urine, which makes urine turn dark when it is exposed to air.

Other Names for This Gene

- AKU
- HGD_HUMAN
- HGO
- homogentisate 1,2-dioxygenase (homogentisate oxidase)
- Homogentisic acid oxidase
- homogentisicase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of HGD (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3081[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28homogentisate+1,2-dioxygenase%5BTIAB%5D%29+OR+%28%28homogentisate+1,2-dioxygenase%5BTIAB%5D%29+OR+%28homogentisicase%5BTIAB%5D%29+OR+%28Homogentisic+acid+oxidase%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- HOMOGENTISATE 1,2-DIOXYGENASE; HGD (https://omim.org/entry/607474)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3081)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=HGD[gene])

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Genomic Location

The *HGD* gene is found on chromosome 3 (https://medlineplus.gov/genetics/chromosome/3/).

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