HPD gene

4-hydroxyphenylpyruvate dioxygenase

Normal Function

The *HPD* gene provides instructions for making an enzyme called 4-hydroxyphenylpyruvate dioxygenase. This enzyme is abundant in the liver, and smaller amounts are found in the kidneys. It is second in a series of five enzymes that work to break down the amino acid tyrosine, a protein building block found in many foods. Specifically, 4-hydroxyphenylpyruvate dioxygenase converts a tyrosine byproduct called 4-hydroxyphenylpyruvate to homogentisic acid. Continuing the process, homogentisic acid is further broken down and ultimately smaller molecules are produced 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

Researchers have identified at least six *HPD* gene mutations that cause tyrosinemia type III. This condition is characterized by neurological problems such as intellectual disability, seizures, and periodic loss of balance and coordination (intermittent ataxia). Some of the mutations that cause this condition change single amino acids in the 4-hydroxyphenylpyruvate dioxygenase enzyme. Other mutations lead to the production of an unusually small enzyme. As a result of these mutations, the activity of the 4-hydroxyphenylpyruvate dioxygenase enzyme is unusually low or absent. As a result, the enzyme cannot perform its role in the breakdown of tyrosine, so 4-hydroxyphenylpyruvate is converted to toxic compounds instead of homogentisic acid. As these toxic compounds builds up in cells, they can impair function and eventually cause cell death. Cells in the nervous system are particularly sensitive to this toxic accumulation. Nerve cell damage and death likely lead to the characteristic features of tyrosinemia type III.

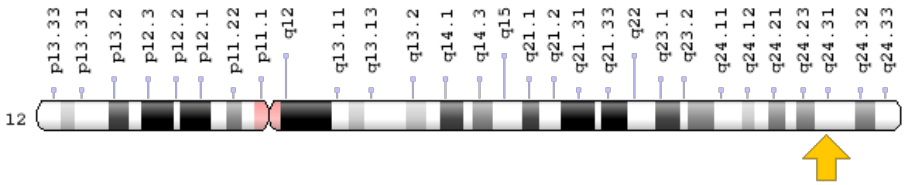
Other disorders

At least two *HPD* gene mutations have been found to cause a rare condition called hawkinsinuria. In infants, this condition is characterized by a failure to gain weight and grow at the expected rate (failure to thrive) and abnormally high acid levels in the blood (acidosis). The *HPD* gene mutations that cause hawkinsinuria result in decreased enzyme activity so that 4-hydroxyphenylpyruvate is not efficiently converted to homogentisic acid. Instead, some 4-hydroxyphenylpyruvate forms an unusual sulfur-containing amino acid called hawkinsin. It remains unclear how the production of hawkinsin leads to the features of hawkinsinuria.

Chromosomal Location

Cytogenetic Location: 12q24.31, which is the long (q) arm of chromosome 12 at position 24.31

Molecular Location: base pairs 121,839,527 to 121,888,611 on chromosome 12 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- 4-HPPD
- 4HPPD
- GLOD3
- HPPD_HUMAN
- P-hydroxyphenylpyruvate hydroxylase
- P-hydroxyphenylpyruvate oxidase
- PPD

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Phenylalanine and Tyrosine Degradation (figure) https://www.ncbi.nlm.nih.gov/books/NBK22453/figure/A3256/?report=objectonly

Clinical Information from GeneReviews

- Tyrosinemia Type I https://www.ncbi.nlm.nih.gov/books/NBK1515

Scientific Articles on PubMed

- PubMed https://www.ncbi.nlm.nih.gov/pubmed?term=%28%284-hydroxyphenylpyruvate+dioxygenase%5BTIAB%5D%29+OR+%28HPD+AND+tyrosinemia%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

- 4-HYDROXYPHENYLPYRUVATE DIOXYGENASE
  http://omim.org/entry/609695
- HAWKINSINURIA
  http://omim.org/entry/140350

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HPD%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:5147
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3242
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3242
- UniProt
  https://www.uniprot.org/uniprot/P32754

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