

PHGDH gene

phosphoglycerate dehydrogenase

Normal Function

The *PHGDH* gene provides instructions for making the parts (subunits) that make up the phosphoglycerate dehydrogenase enzyme. Four PHGDH subunits combine to form the enzyme. This enzyme is involved in the production (synthesis) of the protein building block (amino acid) serine. Specifically, the enzyme converts a substance called 3-phosphoglycerate to 3-phosphohydroxypyruvate in the first step in serine production. Serine is necessary for the development and function of the brain and spinal cord (central nervous system). Serine is a part of chemical messengers called neurotransmitters that transmit signals in the nervous system. Proteins that form cell membranes and the fatty layer of insulation (myelin) that surrounds many nerves also contain serine.

Serine can be obtained from the diet, but brain cells must produce their own serine because dietary serine cannot cross the protective barrier that allows only certain substances to pass between blood vessels and the brain (the blood-brain barrier).

Health Conditions Related to Genetic Changes

Phosphoglycerate dehydrogenase deficiency

At least eight mutations in the *PHGDH* gene have been found to cause phosphoglycerate dehydrogenase deficiency. This condition is characterized by an unusually small head size (microcephaly), severe developmental delay, and recurrent seizures that are difficult to treat (intractable epilepsy). Most of the mutations that cause this condition change single amino acids in the phosphoglycerate dehydrogenase enzyme. The mutations result in the production of an enzyme with decreased function. As a result, less 3-phosphoglycerate is converted into 3-phosphohydroxypyruvate than normal and serine production is stalled at the first step. The lack of serine likely prevents the production of proteins and neurotransmitters in the brain and impairs the formation of normal cells and myelin. These disruptions in normal brain development lead to microcephaly, severe developmental delay, and the other signs and symptoms of phosphoglycerate dehydrogenase deficiency.

Other Names for This Gene

- 3-PGDH
- 3-phosphoglycerate dehydrogenase
- 3PGDH
- D-3-phosphoglycerate dehydrogenase
- epididymis secretory protein Li 113
- HEL-S-113
- PDG
- PGAD
- PGD
- PGDH
- SERA

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PHGDH ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=26227\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=26227[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28PHGDH%5BTIAB%5D%29+OR+%28phosphoglycerate+dehydrogenase%5BTIAB%5D%29%29+OR+%28%283-phosphoglycerate+dehydrogenase%5BTIAB%5D%29+OR+%283-PGDH%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- PHOSPHOGLYCERATE DEHYDROGENASE; PHGDH (<https://omim.org/entry/606879>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/26227>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=PHGDH\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=PHGDH[gene]))

References

- de Koning TJ, Klomp LW. Serine-deficiency syndromes. *Curr Opin Neurol*. 2004Apr; 17(2):197-204. doi: 10.1097/00019052-200404000-00019. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15021249>)
- Fuchs SA, Dorland L, de Sain-van der Velden MG, Hendriks M, Klomp LW, Berger R, de Koning TJ. D-serine in the developing human central nervous system. *Ann Neurol*. 2006 Oct;60(4):476-80. doi: 10.1002/ana.20977. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17068790>)
- Tabatabaie L, de Koning TJ, Geboers AJ, van den Berg IE, Berger R, Klomp LW. Novel mutations in 3-phosphoglycerate dehydrogenase (PHGDH) are distributed throughout the protein and result in altered enzyme kinetics. *Hum Mutat*. 2009May;30(5):749-56. doi: 10.1002/humu.20934. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19235232>)

Genomic Location

The *PHGDH* gene is found on chromosome 1 (<https://medlineplus.gov/genetics/chromosome/1/>).

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