GPHN gene

gephyrin

Normal Function

The *GPHN* gene provides instructions for making a protein called gephyrin, which has two major functions in the body: the protein aids in the formation (biosynthesis) of a molecule called molybdenum cofactor, and it also plays a role in communication between nerve cells (neurons).

Gephyrin performs the final two steps in molybdenum cofactor biosynthesis. Molybdenum cofactor, which contains the element molybdenum, is essential to the function of several enzymes called sulfite oxidase, aldehyde oxidase, xanthine dehydrogenase, and mitochondrial amidoxime reducing component (mARC). These enzymes help break down (metabolize) different substances in the body, some of which are toxic if not metabolized.

Gephyrin also plays an important role in neurons. Communication between neurons depends on chemicals called neurotransmitters. To relay signals, a neuron releases neurotransmitters, which attach to receptor proteins on neighboring neurons. Gephyrin anchors certain receptor proteins to the correct location in neurons so that the receptors can receive the signals relayed by neurotransmitters.

Health Conditions Related to Genetic Changes

Molybdenum cofactor deficiency

GPHN gene mutations cause a disorder called molybdenum cofactor deficiency. This disorder is characterized by seizures that begin early in life and brain dysfunction that worsens over time (encephalopathy); the condition is usually fatal by early childhood. At least two mutations in the *GPHN* gene have been found to cause a form of the disorder designated type C or complementation group C. This is the rarest form of the condition, affecting only a small number of individuals.

The *GPHN* gene mutations involved in molybdenum cofactor deficiency likely reduce or eliminate the function of gephyrin. The known mutations impair gephyrin's ability to perform one or both of the final two steps of molybdenum cofactor biosynthesis. Without the cofactor, the metabolic enzymes that rely on it cannot function.

The resulting loss of enzyme activity leads to buildup of certain chemicals, including

sulfite, S-sulfocysteine, xanthine, and hypoxanthine, and low levels of another chemical called uric acid. (Testing for these chemicals can help in the diagnosis of this condition.) Sulfite, which is normally broken down by sulfite oxidase, is toxic, especially to the brain. Researchers suggest that damage caused by the abnormally high levels of sulfite (and possibly other chemicals) leads to encephalopathy, seizures, and the other features of molybdenum cofactor deficiency.

Other Names for This Gene

- GEPH
- gephyrin isoform 1
- gephyrin isoform 2
- GPH
- GPHRYN
- HKPX1
- KIAA1385
- MOCODC

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of GPHN (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=10243[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28GPHN%5BTIAB%5D%29+OR+%28gephyrin%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- GEPHYRIN; GPHN (https://omim.org/entry/603930)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/10243)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=GPHN[gene])

References

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Genomic Location

The *GPHN* gene is found on chromosome 14 (https://medlineplus.gov/genetics/chromosome/14/).

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