HEXB gene

hexosaminidase subunit beta

Normal Function

The *HEXB* gene provides instructions for making a protein that is one part (the beta subunit) of two related enzymes, beta-hexosaminidase A and beta-hexosaminidase B. Each of these enzymes is made up of two subunits. Beta-hexosaminidase A includes one alpha subunit (produced from the *HEXA* gene) and one beta subunit. Beta-hexosaminidase B is composed of two beta subunits.

Beta-hexosaminidase A and beta-hexosaminidase B play a critical role in nerve cells (neurons) in the brain and spinal cord (central nervous system). In neurons, these enzymes are found in lysosomes, which are structures in cells that break down toxic substances and act as recycling centers. Within lysosomes, the beta-hexosaminidase A and B enzymes break down fatty compounds called sphingolipids, complex sugars called oligosaccharides, and molecules that are linked to sugars (such as glycoproteins). In particular, beta-hexosaminidase A forms part of a complex that breaks down a fatty substance called GM2 ganglioside.

Health Conditions Related to Genetic Changes

Sandhoff disease

Sandhoff disease is caused by variants (also known as mutations) in the *HEXB* gene. These variants reduce or eliminate the activity of both beta-hexosaminidase A and beta-hexosaminidase B. A reduction in enzyme activity results in an inability to properly break down GM2 ganglioside and other molecules, which allows these compounds to accumulate within cells. Increased levels of GM2 ganglioside are particularly toxic to neurons in the central nervous system. Excess GM2 ganglioside leads to the progressive destruction of these cells, which causes many of the characteristic features of Sandhoff disease.

Most of the known variants in the *HEXB* gene cause the severe form of Sandhoff disease, which becomes apparent in infancy. These variants prevent cells from making any beta-hexosaminidase A or beta-hexosaminidase B, or lead to the production of completely nonfunctional versions of these enzymes. The most common variant deletes a large segment of DNA near the beginning of the *HEXB* gene, which results in a total loss of enzyme activity. Other variants reduce but do not eliminate the activity of the

enzymes; these genetic changes are responsible for the less severe forms of Sandhoff disease, which appear later in life.

Other Names for This Gene

- beta-N-acetylhexosaminidase B
- ENC-1AS
- Hex B
- HEXB_HUMAN
- hexosaminidase B
- hexosaminidase B (beta polypeptide)

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of HEXB (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3074[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=((HEXB%5BTIAB%5D)+OR+(hexosaminidase+B%5BTIAB%5D))+AND+((Genes%5BMH%5D)+OR+(Genetic+Phenomena%5BMH%5D))+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- HEXOSAMINIDASE B; HEXB (https://omim.org/entry/606873)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3074)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=HEXB[gene])

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Genomic Location

The *HEXB* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

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