HEXA gene

hexosaminidase subunit alpha

Normal Function

The *HEXA* gene provides instructions for making one part (subunit) of an enzyme called beta-hexosaminidase A. Specifically, the protein produced from the *HEXA* gene forms the alpha subunit of this enzyme. One alpha subunit joins with one beta subunit (produced from the *HEXB* gene) to form a functioning beta-hexosaminidase A enzyme.

Beta-hexosaminidase A plays a critical role in the brain and spinal cord (central nervous system). This enzyme is found in lysosomes, which are structures in cells that break down toxic substances and act as recycling centers. Within lysosomes, beta-hexosaminidase A forms part of a complex that breaks down a fatty substance called GM2 ganglioside found in cell membranes.

Health Conditions Related to Genetic Changes

Tay-Sachs disease

More than 210 variants (also known as mutations) that cause Tay-Sachs disease have been identified in the *HEXA* gene. Tay-Sachs disease is a condition that is characterized by movement disorders, intellectual and developmental disability, and other neurological problems caused by the death of nerve cells (neurons) in the central nervous system.

The *HEXA* gene variants that cause Tay-Sachs disease eliminate or severely reduce the activity of the enzyme beta-hexosaminidase A. This lack of enzyme activity prevents the enzyme from breaking down GM2 ganglioside. As a result, this substance builds up to toxic levels, particularly in neurons in the central nervous system. Progressive damage caused by the buildup of GM2 ganglioside leads to the destruction of these cells, which causes the signs and symptoms of Tay-Sachs disease.

Most of the known *HEXA* gene variants result in a completely nonfunctional version of beta-hexosaminidase A. These variants cause a severe form of Tay-Sachs disease, known as infantile Tay-Sachs disease, which appears in infancy. Other variants severely reduce but do not eliminate the activity of beta-hexosaminidase A. These genetic changes are responsible for less severe forms of Tay-Sachs disease, known as the juvenile and late-onset forms, which appear later in life.

Other Names for This Gene

- Beta-hexosaminidase A
- beta-N-Acetylhexosaminidase A
- Hex A
- HEXA_HUMAN
- hexosaminidase A (alpha polypeptide)
- N-acetyl-beta-glucosaminidase

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of HEXA (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3073[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28HEXA+AND+hexosaminidase%5BTIAB%5D%29+OR+%28hexosaminidase+A%5BTIAB%5D%29%29+OR+%28%28Beta-hexosaminidase+A%5BTIAB%5D%29+OR+%28beta-N-Acetylhexosaminidase+A%5BTIAB%5D%29+OR+%28N-acetyl-beta-glucosaminidase%5BTIAB%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

- HEXOSAMINIDASE A; HEXA (https://omim.org/entry/606869)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3073)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=HEXA[gene])

References

- Dersh D, Iwamoto Y, Argon Y. Tay-Sachs disease mutations in HEXA target the alphachain of hexosaminidase A to endoplasmic reticulum-associated degradation. MolBiol Cell. 2016 Dec 1;27(24):3813-3827. doi: 10.1091/mbc.E16-01-0012. Epub 2016Sep 28. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/27682588)
- Lemieux MJ, Mark BL, Cherney MM, Withers SG, Mahuran DJ, James MN. Crystallographic structure of human beta-hexosaminidase A: interpretation ofTay-Sachs mutations and loss of GM2 ganglioside hydrolysis. J Mol Biol. 2006 Jun16;

359(4):913-29. doi: 10.1016/j.jmb.2006.04.004. Epub 2006 Apr 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16698036) or Free article on PubMed Central (https ://www.ncbi.nlm.nih.gov/pmc/articles/PMC2910082/)

- Matsuzawa F, Aikawa S, Sakuraba H, Lan HT, Tanaka A, Ohno K, Sugimoto Y, Ninomiya H, Doi H. Structural basis of the GM2 gangliosidosis B variant. J HumGenet. 2003;48(11):582-9. doi: 10.1007/s10038-003-0082-7. Epub 2003 Oct 24. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14577003)
- Montalvo AL, Filocamo M, Vlahovicek K, Dardis A, Lualdi S, Corsolini F, BembiB, Pittis MG. Molecular analysis of the HEXA gene in Italian patients withinfantile and late onset Tay-Sachs disease: detection of fourteen novel alleles.Hum Mutat. 2005 Sep;26(3):282. doi: 10.1002/humu.9363. Citation on PubMed (https://pubmed.ncbi.nl m.nih.gov/16088929)
- Myerowitz R, Lawson D, Mizukami H, Mi Y, Tifft CJ, Proia RL. Molecularpathophysiology in Tay-Sachs and Sandhoff diseases as revealed by gene expressionprofiling. Hum Mol Genet. 2002 May 15;11(11):1343-50. doi:10.1093/hmg/ 11.11.1343. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12019216)
- Toro C, Shirvan L, Tifft C. HEXA Disorders. 1999 Mar 11 [updated 2020Oct 1]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A,editors. GeneReviews(R) [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1218/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301397)

Genomic Location

The *HEXA* gene is found on chromosome 15 (https://medlineplus.gov/genetics/chromos ome/15/).

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