GBE1 gene

1,4-alpha-glucan branching enzyme 1

Normal Function

The *GBE1* gene provides instructions for making the glycogen branching enzyme. This enzyme is involved in the last step of the production of a complex sugar called glycogen, which is a major source of stored energy in the body. Glycogen is made up of many molecules of a simple sugar called glucose; some glucose molecules are linked together in a straight line, while others branch off the main line and form side chains. The glycogen branching enzyme is involved in the formation of these side chains. The branched structure of glycogen makes it more compact for storage and allows it to break down more easily when it is needed for fuel.

Health Conditions Related to Genetic Changes

Adult polyglucosan body disease

At least three mutations in the *GBE1* gene have been found to cause adult polyglucosan body disease, a condition that affects the nervous system. These mutations change single protein building blocks (amino acids) in the glycogen branching enzyme. One mutation appears to be more common in affected people with Ashkenazi Jewish ancestry. This mutation replaces the amino acid tyrosine with the amino acid serine at position 329 in the enzyme (written Tyr329Ser or Y329S).

Most mutations that cause adult polyglucosan body disease lead to a shortage (deficiency) of the enzyme. As a result, glycogen has fewer side chains. These abnormal glycogen molecules, called polyglucosan bodies, accumulate within cells and cause damage. Nerve cells (neurons) appear to be particularly vulnerable to the accumulation of polyglucosan bodies in this disorder. Damage to neurons causes reduced sensation, weakness, and other nervous system problems in people with adult polyglucosan body disease.

Glycogen storage disease type IV

Approximately 40 mutations in the *GBE1* gene have been found to cause glycogen storage disease type IV (GSD IV). This disorder is characterized by liver and muscle problems that usually begin in infancy and are caused by a buildup of abnormal glycogen. Most of the mutations that cause this condition change single amino acids in

the glycogen branching enzyme.

The *GBE1* gene mutations that cause GSD IV lead to a severe shortage or complete absence of glycogen branching enzyme. As a result, polyglucosan bodies accumulate in cells, leading to damage and cell death. Polyglucosan bodies build up in cells throughout the body, but liver cells and muscle cells are most severely affected in GSD IV. Glycogen accumulation in the liver interferes with liver functioning, causing an enlarged liver and liver disease. The inability of muscle cells to break down glycogen for energy leads to muscle weakness and wasting.

It is unclear why liver and muscle cells are affected by the accumulation of polyglucosan bodies in GSD IV, while neurons are solely affected in adult polyglucosan body disease (described above).

Other Names for This Gene

- amylo-(1,4 to 1,6) transglucosidase
- amylo-(1,4 to 1,6) transglycosylase
- GBE
- GLGB_HUMAN
- glucan (1,4-alpha-), branching enzyme 1
- glycogen branching enzyme

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of GBE1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2632[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28GBE1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2160+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- GLYCOGEN BRANCHING ENZYME; GBE1 (https://omim.org/entry/607839)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/2632)

- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=GBE1[gene])

References

- Bruno C, van Diggelen OP, Cassandrini D, Gimpelev M, Giuffre B, Donati MA, Introvini P, Alegria A, Assereto S, Morandi L, Mora M, Tonoli E, Mascelli S,Traverso M, Pasquini E, Bado M, Vilarinho L, van Noort G, Mosca F, DiMauro S,Zara F, Minetti C. Clinical and genetic heterogeneity of branching enzymedeficiency (glycogenosis type IV). Neurology. 2004 Sep 28;63(6):1053-8. doi:10.1212/01.wnl. 0000138429.11433.0d. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15452 297)
- Klein CJ, Boes CJ, Chapin JE, Lynch CD, Campeau NG, Dyck PJ, Dyck PJ. Adultpolyglucosan body disease: case description of an expanding genetic and clinicalsyndrome. Muscle Nerve. 2004 Feb;29(2):323-8. doi: 10.1002/mus.10520. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14755501)
- Lossos A, Meiner Z, Barash V, Soffer D, Schlesinger I, Abramsky O, Argov Z, Shpitzen S, Meiner V. Adult polyglucosan body disease in Ashkenazi Jewishpatients carrying the Tyr329Ser mutation in the glycogen-branching enzyme gene.Ann Neurol. 1998 Dec;44(6):867-72. doi: 10.1002/ana.410440604. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9851430)
- Massa R, Bruno C, Martorana A, de Stefano N, van Diggelen OP, Federico A.Adult polyglucosan body disease: proton magnetic resonance spectroscopy of thebrain and novel mutation in the GBE1 gene. Muscle Nerve. 2008 Apr;37(4):530-6.doi: 10. 1002/mus.20916. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17994551)
- Mochel F, Schiffmann R, Steenweg ME, Akman HO, Wallace M, Sedel F, Laforet P, Levy R, Powers JM, Demeret S, Maisonobe T, Froissart R, Da Nobrega BB, Fogel BL,Natowicz MR, Lubetzki C, Durr A, Brice A, Rosenmann H, Barash V, Kakhlon O, Gomori JM, van der Knaap MS, Lossos A. Adult polyglucosan body disease: NaturalHistory and Key Magnetic Resonance Imaging Findings. Ann Neurol. 2012Sep;72(3):433-41. doi: 10.1002/ana.23598. Citation on PubMed (https://pubme d.ncbi.nlm.nih.gov/23034915) or Free article on PubMed Central (https://www.ncbi.nl m.nih.gov/pmc/articles/PMC4329926/)
- Moses SW, Parvari R. The variable presentations of glycogen storage diseasetype IV: a review of clinical, enzymatic and molecular studies. Curr Mol Med.2002 Mar;2(2):177-88. doi: 10.2174/1566524024605815. Citation on PubMed (https://pubmed.nc bi.nlm.nih.gov/11949934)
- Nolte KW, Janecke AR, Vorgerd M, Weis J, Schroder JM. Congenital type IVglycogenosis: the spectrum of pleomorphic polyglucosan bodies in muscle, nerve, and spinal cord with two novel mutations in the GBE1 gene. Acta Neuropathol. 2008Nov;116(5):491-506. doi: 10.1007/s00401-008-0417-8. Epub 2008 Jul 26. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18661138)

Genomic Location

The *GBE1* gene is found on chromosome 3 (https://medlineplus.gov/genetics/chromosome/3/).

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