

## GLB1 gene

galactosidase beta 1

### Normal Function

The *GLB1* gene provides instructions for producing two different proteins. The primary protein produced from the *GLB1* gene is an enzyme called beta-galactosidase ( $\beta$ -galactosidase). This enzyme is located in lysosomes, which are compartments within cells that break down and recycle different types of molecules.  $\beta$ -galactosidase helps break down certain substances, including GM1 ganglioside and keratan sulfate. GM1 ganglioside is important for normal functioning of nerve cells (neurons) in the brain. Keratan sulfate is particularly abundant in cartilage and the clear covering of the eye (cornea). Keratan sulfate belongs to a group of large sugar molecules called glycosaminoglycans or mucopolysaccharides.

The *GLB1* gene also provides instructions for making the elastin-binding protein. This protein is smaller than  $\beta$ -galactosidase and is found on the surface of cells rather than in lysosomes. Elastin-binding protein interacts with other proteins called cathepsin A and neuraminidase 1. This group of proteins forms the elastin receptor complex. This complex plays a role in building elastic fibers, which are a component of the connective tissue that forms the body's supportive framework.

### Health Conditions Related to Genetic Changes

#### GM1 gangliosidosis

Many variants (also called mutations) in the *GLB1* gene have been found to cause GM1 gangliosidosis. The signs and symptoms of this condition primarily result from the loss of neurons in the brain and spinal cord over time. Most variants change single DNA building blocks (nucleotides) in the *GLB1* gene. These variants often affect the production of both  $\beta$ -galactosidase and elastin-binding protein.

The *GLB1* gene variants that cause GM1 gangliosidosis produce versions of  $\beta$ -galactosidase that are not as effective at breaking down GM1 ganglioside and keratan sulfate as the normal version of the enzyme. As a result, these substances build up to toxic levels in many tissues and organs. In the brain, damage caused by the buildup of GM1 ganglioside leads to the loss of neurons, which causes intellectual disability, movement problems, and many of the signs and symptoms of GM1 gangliosidosis.

It is not clear how changes in the elastin-binding protein affect the development of GM1 gangliosidosis. The altered protein may cause the weakened heart muscle (cardiomyopathy) found in some people with GM1 gangliosidosis.

### Mucopolysaccharidosis type IV

Variants in the *GLB1* gene have been found to cause mucopolysaccharidosis type IV (MPS IV). This is a progressive condition that mainly affects the skeleton. Most of the variants that cause MPS IV change single nucleotides in the *GLB1* gene. All of the variants that cause MPS IV disrupt the breakdown of keratan sulfate by  $\beta$ -galactosidase. The breakdown of GM1 ganglioside is not affected by these variants.

Because keratan sulfate is predominantly found in cartilage and the cornea, the buildup of this substance causes skeletal abnormalities and cloudy corneas. Researchers believe that a buildup of glycosaminoglycans may also cause the features of MPS IV by interfering with the functions of other proteins inside lysosomes and disrupting the movement of molecules inside the cell.

### **Other Names for This Gene**

- BGAL\_HUMAN
- EBP
- elastin receptor 1, 67kDa
- ELNR1

### **Additional Information & Resources**

#### Tests Listed in the Genetic Testing Registry

- Tests of GLB1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2720\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2720[geneid]))

#### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28GLB1%5BTIAB%5D%29+OR+%28%28beta-galactosidase%5BTIAB%5D%29+OR+%28acid+beta-galactosidase%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+720+days%22%5Bdp%5D%29%29%29>)

#### Catalog of Genes and Diseases from OMIM

- GALACTOSIDASE, BETA-1; GLB1 (<https://omim.org/entry/611458>)

#### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/2720>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=GLB1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=GLB1[gene]))

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## Genomic Location

The *GLB1* gene is found on chromosome 3 (<https://medlineplus.gov/genetics/chromosome/3/>).

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