GLB1 Gene

Subjects: Genetics & Heredity
Contributor: Vivi Li

Galactosidase beta 1

Keywords: genes

1. Normal Function

The *GLB1* gene provides instructions for producing an enzyme called beta-galactosidase (β-galactosidase). This enzyme is located in lysosomes, which are compartments within cells that break down and recycle different types of molecules. Within lysosomes, β-galactosidase helps break down certain molecules, including substances called GM1 ganglioside and keratan sulfate. GM1 ganglioside is important for normal functioning of nerve cells in the brain, and 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 (GAGs) or mucopolysaccharides.

The *GLB1* gene also provides instructions for making the elastin-binding protein. On the cell surface, elastin-binding protein interacts with proteins called cathepsin A and neuraminidase 1 to form the elastin receptor complex. This receptor complex plays a role in the formation of elastic fibers, which are a component of the connective tissue that forms the body's supportive framework.

2. Health Conditions Related to Genetic Changes

2.1 GM1 Gangliosidosis

More than 80 mutations in the *GLB1* gene have been found to cause GM1 gangliosidosis. Most mutations change single DNA building blocks (nucleotides) in the *GLB1* gene. These mutations often affect the production of both β-galactosidase and elastin-binding protein.

GLB1 gene mutations that cause GM1 gangliosidosis reduce or eliminate the activity of β-galactosidase. Without enough functional β-galactosidase, GM1 ganglioside and keratan sulfate cannot be broken down. As a result, these substances accumulate to toxic levels in many tissues and organs. In the brain, progressive damage caused by the buildup of GM1 ganglioside leads to the destruction of nerve cells, which causes many of the signs and symptoms of GM1 gangliosidosis.

Although the role elastin-binding protein plays in the development of GM1 gangliosidosis is unclear, the alteration of this protein may contribute to the weakened heart muscle (cardiomyopathy) found in some people with GM1 gangliosidosis.

2.2 Mucopolysaccharidosis Type IV

More than 10 mutations in the *GLB1* gene have been found to cause mucopolysaccharidosis type IV (MPS IV). Most of these mutations change single nucleotides in the gene. All of the mutations that cause MPS IV disrupt the breakdown of keratan sulfate by β-galactosidase. The degradation of GM1 ganglioside is not affected by these mutations.

The lack of β-galactosidase activity leads to the accumulation of keratan sulfate within lysosomes. 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 GAGs 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.

3. Other Names for This Gene

- acid beta-galactosidase
- beta-galactosidase

- beta-galactosidase isoform a preproprotein
- beta-galactosidase isoform b
- beta-galactosidase isoform c preproprotein
- BGAL_HUMAN
- EBP
- elastin receptor 1, 67kDa
- ELNR1
- galactosidase, beta 1
- lactase

References

1. Brunetti-Pierri N, Scaglia F. GM1 gangliosidosis: review of clinical,molecular, and therapeutic aspects. Mol Genet Meta b. 2008 Aug;94(4):391-6. doi:10.1016/j.ymgme.2008.04.012.
2. Duca L, Blanchevoye C, Cantarelli B, Ghoneim C, Dedieu S, Delacoux F,Hornebeck W, Hinek A, Martiny L, Debelle L. The elastin receptor complextransduces signals through the catalytic activity of its Neu-1 subunit. J BiolChem. 2007 Ap r 27;282(17):12484-91.
3. Hofer D, Paul K, Fantur K, Beck M, Bürger F, Caillaud C, Fumic K, Ledvinova J,Lugowska A, Michelakakis H, Radeva B, Ramaswami U, Plecko B, Paschke E. GM1gangliosidosis and Morquio B disease: expression analysis of missense mutationsaffecting the catalytic site of acid beta-galactosidase. Hum Mutat. 2009Aug;30(8):1214-21. doi: 10.1002/hum u.21031.
4. Hofer D, Paul K, Fantur K, Beck M, Roubergue A, Vellodi A, Poorthuis BJ,Michelakakis H, Plecko B, Paschke E. Pheno type determining alleles in GM1gangliosidosis patients bearing novel GLB1 mutations. Clin Genet. 2010Sep;78(3):236-46. doi: 10.1111/j.1399-0004.2010.01379.x.
5. Santamaria R, Chabás A, Callahan JW, Grinberg D, Vilageliu L. Expression andcharacterization of 14 GLB1 mutant all eles found in GM1-gangliosidosis andMorquio B patients. J Lipid Res. 2007 Oct;48(10):2275-82.
6. Santamaria R, Chabás A, Coll MJ, Miranda CS, Vilageliu L, Grinberg D.Twenty-one novel mutations in the GLB1 gene i dentified in a large group ofGM1-gangliosidosis and Morquio B patients: possible common origin for theprevalent p.R59 H mutation among gypsies. Hum Mutat. 2006 Oct;27(10):1060.