PEX1 Gene

Subjects: Genetics & Heredity
Contributor: Lily Guo

peroxisomal biogenesis factor 1

genes

1. Introduction

The *PEX1* gene provides instructions for making a protein called peroxisomal biogenesis factor 1 (Pex1p), which is part of a group of proteins called peroxins. Peroxins are essential for the formation and normal functioning of cell structures called peroxisomes. Peroxisomes are sac-like compartments that contain enzymes needed to break down many different substances, including fatty acids and certain toxic compounds. They are also important for the production of fats (lipids) used in digestion and in the nervous system. Peroxins assist in the formation (biogenesis) of peroxisomes by producing the membrane that separates the peroxisome from the rest of the cell and by importing enzymes into the peroxisome. Pex1p enables other peroxins to bring enzymes into the peroxisome.

2. Health Conditions Related to Genetic Changes

2.1. Zellweger spectrum disorder

At least 114 mutations in the *PEX1* gene have been identified in people with Zellweger spectrum disorder, which is a group of conditions that have overlapping signs and symptoms and affect many parts of the body. The conditions' features, which vary in severity, can include weak muscle tone (hypotonia), developmental delay, and vision and hearing problems. Mutations in the *PEX1* gene are the most common cause of Zellweger spectrum disorder and are found in nearly 70 percent of affected individuals.

There are two common *PEX1* gene mutations found in people with Zellweger spectrum disorder. One mutation replaces the protein building block (amino acid) glycine with the amino acid aspartic acid at position 843 in Pex1p (written as Gly843Asp or G843D). This mutation leads to reduced levels of the protein. Individuals who have the G843D mutation tend to have signs and symptoms that are at the less-severe end of the condition spectrum. The other common mutation, which is known as the 1700fs mutation, leads to the production of an abnormally short, nonfunctional Pex1p. People who have the 1700fs mutation often have signs and symptoms that are at the severe end of the condition spectrum.

Mutations in the *PEX1* gene that cause Zellweger spectrum disorder reduce or eliminate the activity of the Pex1p protein. Without enough functional Pex1p, enzymes are not properly imported into peroxisomes. As a result, cells contain empty peroxisomes that cannot carry out their usual functions. The severe end of the condition spectrum is caused by the absence of functional peroxisomes within cells. The less severe end of the condition spectrum results from mutations that allow some peroxisomes to form.

3. Other Names for This Gene

- peroxin1
- peroxisome biogenesis disorder protein 1
- PEX1_HUMAN
- Pex1p
- ZWS1

References

1. Crane DI, Maxwell MA, Paton BC. PEX1 mutations in the Zellweger spectrum ofthe peroxisome biogenesis disorders. Hum Mutat. 2005 Sep;26(3):167-75. Review.
2. Ebberink MS, Mooijer PA, Gootjes J, Koster J, Wanders RJ, Waterham HR. Geneticclassification and mutational spectrum of more than 600 patients with a Zellwegersyndrome spectrum disorder. Hum Mutat. 2011 Jan;32(1):59-69. doi:10.1002/humu.21388.
3. Fujiki Y, Miyata N, Matsumoto N, Tamura S. Dynamic and functional assembly of the AAA peroxins, Pex1p and Pex6p, and their membrane receptor Pex26p involved inshuttling of the PTS1 receptor Pex5p in peroxisome biogenesis. Biochem Soc Trans.2008 Feb;36(Pt 1):109-13. doi: 10.1042/BST0360109. Review.
4. Rosenkranz K, Birschmann I, Grunau S, Girzalsky W, Kunau WH, Erdmann R.Functional association of the AAA complex and the peroxisomal importomer. FEBS J.2006 Aug;273(16):3804-15.
5. Rosewich H, Ohlenbusch A, Gärtner J. Genetic and clinical aspects of Zellwegerspectrum patients with PEX1 mutations. J Med Genet. 2005 Sep;42(9):e58.
6. Steinberg SJ, Raymond GV, Braverman NE, Moser AB. Zellweger Spectrum Disorder.2003 Dec 12 [updated 2020 Oct 29]. In: Adam MP, Ardinger HH, Pagon RA, WallaceSE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet]. Seattle(WA): University of Washington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1448/
7. Thoms S, Erdmann R. Peroxisomal matrix protein receptor ubiquitination andrecycling. Biochim Biophys Acta. 2006 Dec;1763(12):1620-8.Review.

8. Wanders RJ, Waterham HR. Peroxisomal disorders I: biochemistry and genetics ofperoxisome biogenesis disorders. Clin Genet. 2005 Feb;67(2):107-33. Review.