LIPA Gene

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1. Introduction

The *LIPA* gene provides instructions for producing an enzyme called lysosomal acid lipase. This enzyme is found in cell compartments called lysosomes, which digest and recycle materials the cell no longer needs. Lysosomal acid lipase breaks down fats (lipids) such as triglycerides and cholesteryl esters. Cholesteryl esters are made up of two lipids that are attached to each other, cholesterol and a fatty acid. Lysosomal acid lipase separates the cholesterol from the fatty acid. Triglycerides are stored fats that can be broken down into fatty acids that are used for energy. The lipids produced from these processes are used by the body or transported to the liver for removal.

2. Health Conditions Related to Genetic Changes

2.1. Lysosomal Acid Lipase Deficiency

Approximately 60 mutations in the *LIPA* gene have been found to cause lysosomal acid lipase deficiency. This inherited condition is characterized by the accumulation of harmful amounts of lipids in cells and tissues throughout the body. Mutations in the *LIPA* gene lead to a shortage (deficiency) of functional lysosomal acid lipase. The severity of the condition depends on how much working enzyme is available. In individuals with a complete loss of enzyme activity, the condition begins in infancy and is often fatal. In individuals with some remaining enzyme activity, the amount of enzyme activity generally determines the severity of the condition.

The most common *LIPA* gene mutation, found in about half of individuals with lysosomal acid lipase deficiency that begins in childhood or later, disrupts the way the gene's instructions are used to make lysosomal acid lipase. This particular mutation, called a splice-site mutation, substitutes the DNA building block (nucleotide) guanine for the nucleotide adenine near an area of the gene called exon 8 (written as IVS8-1G>A). This mutation results in the deletion of 24 protein building blocks (amino acids). People with the IVS8-1G>A mutation in both copies of the *LIPA* gene in each cell have 5 percent of the normal amount of lysosomal acid lipase activity.

Reduction or absence of lysosomal acid lipase activity results in the accumulation of triglycerides, cholesteryl esters, and other lipids within lysosomes, causing fat buildup in multiple tissues. The body's inability to produce cholesterol from the breakdown of these lipids leads to an increase in alternative methods of cholesterol production and higher-than-normal levels of cholesterol in the blood. The excess lipids are transported to the liver for removal. Because many of them are not broken down properly, they cannot be removed from the body; instead; they accumulate in the liver, resulting in liver disease. The progressive accumulation of lipids in tissues results in organ dysfunction and the signs and symptoms of lysosomal acid lipase deficiency.

3. Other Names for This Gene

- cholesterol ester hydrolase
- LAL
- LICH_HUMAN
- lipase A
- lipase A, lysosomal acid

- lipase A, lysosomal acid, cholesterol esterase
- lysosomal acid lipase
- sterol esterase

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