TPI1 Gene

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Triosephosphate isomerase 1: The TPI1 gene provides instructions for making an enzyme called triosephosphate isomerase 1.

genes

1. Normal Function

The *TPI1* gene provides instructions for making an enzyme called triosephosphate isomerase 1. This enzyme is involved in a critical energy-producing process known as glycolysis. During glycolysis, the simple sugar glucose is broken down to produce energy for cells. The triosephosphate isomerase 1 enzyme carries out a specific reaction during glycolysis: the conversion of a molecule called dihydroxyacetone phosphate (DHAP) to glyceraldehyde 3-phosphate. This conversion can go both ways, meaning that the triosephosphate isomerase 1 enzyme can also convert glyceraldehyde 3-phosphate back into DHAP. Additional steps convert glyceraldehyde 3-phosphate into other molecules that ultimately produce energy in the form of a molecule called ATP.

For the triosephosphate isomerase 1 enzyme to be turned on (active), it has to attach (bind) to another triosephosphate isomerase 1 enzyme, forming a two-enzyme complex called a dimer.

2. Health Conditions Related to Genetic Changes

2.1. Triosephosphate isomerase deficiency

At least 12 mutations in the *TPI1* gene have been found to cause triosephosphate isomerase deficiency. This condition is characterized by a shortage of red blood cells (anemia), movement problems, increased susceptibility to infection, and muscle weakness that can affect breathing and heart function.

TPI1 gene mutations can lead to the production of an enzyme with decreased activity. As a result, glycolysis is impaired and cells have a decreased supply of energy. One *TPI1* gene mutation accounts for approximately 80 percent of triosephosphate isomerase deficiency cases. This change replaces the protein building block (amino acid) glutamic acid with the amino acid aspartic acid at position 104 in the triosephosphate isomerase 1 enzyme (written as Glu104Asp or E104D). This mutation causes the enzyme to be unstable and impairs its ability to form a dimer and become active.

Red blood cells depend solely on the breakdown of glucose for energy. Without functional triosephosphate isomerase 1 enzyme to convert DHAP to glyceraldehyde 3-phosphate, red blood cells accumulate DHAP, which is toxic in large quantities. Unlike other cells, red blood cells do not have alternative pathways to break down DHAP. Due to the buildup of DHAP and the lack of cellular energy, red blood cells die earlier than normal.

Cells with high energy demands, such as nerve cells in the brain, white blood cells, and heart (cardiac) muscle cells are also susceptible to cell death due to reduced energy caused by impaired glycolysis. Nerve cells in the part of the brain involved in coordinating movements (the cerebellum) are particularly affected in people with triosephosphate isomerase deficiency. Death of red and white blood cells, nerve cells in the brain, and cardiac muscle cells leads to the signs and symptoms of triosephosphate isomerase deficiency.

3. Other Names for This Gene

- TIM
- TPI
- TPID
- triose-phosphate isomerase
- triosephosphate isomerase

References

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