PDHA1 Gene

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pyruvate dehydrogenase E1 alpha 1 subunit

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1. Introduction

The *PDHA1* gene provides instructions for making a protein called E1 alpha. The E1 alpha protein is a piece (a subunit) of a larger protein: two E1 alpha proteins combine with two copies of another protein called E1 beta (produced from the *PDHB* gene) to form the E1 enzyme. This enzyme, also known as pyruvate dehydrogenase, is a component of a group of proteins called the pyruvate dehydrogenase complex.

The pyruvate dehydrogenase complex plays an important role in the pathways that convert the energy from food into a form that cells can use. This complex converts a molecule called pyruvate, which is formed from the breakdown of carbohydrates, into another molecule called acetyl-CoA. The E1 enzyme performs one part of this chemical reaction. The conversion of pyruvate is essential to begin the series of chemical reactions that produces adenosine triphosphate (ATP), the cell's main energy source.

2. Health Conditions Related to Genetic Changes

2.1. Pyruvate dehydrogenase deficiency

Mutations in the *PDHA1* gene are the most common cause of pyruvate dehydrogenase deficiency, accounting for approximately 80 percent of cases of this condition. Pyruvate dehydrogenase deficiency is characterized by a potentially life-threatening buildup of a chemical called lactic acid in the body (lactic acidosis), delayed development, and neurological problems. Dozens of *PDHA1* gene mutations have been identified in affected individuals. These mutations have been divided into two groups. One group includes mutations that add or remove DNA building blocks (nucleotides) to the *PDHA1* gene (called insertion and deletion mutations, respectively). These types of mutations occur more commonly in affected females than males. The other group includes mutations that change single protein building blocks (amino acids) in the E1 alpha protein or result in a premature stop signal in the instructions for making the protein (called missense and nonsense mutations, respectively). These types of mutations occur in affected males more often than females.

Mutations in the *PDHA1* gene associated with pyruvate dehydrogenase deficiency lead to a reduction in the amount of E1 alpha protein or result in an abnormal protein that cannot function properly. The abnormal protein may not be able to interact with E1 beta to form the E1 enzyme or with other factors needed for the E1 enzyme to perform its chemical reaction. A decrease in functional E1 alpha results in reduced pyruvate dehydrogenase complex activity. With decreased function of this complex, pyruvate builds up and is converted, in another chemical reaction, to lactic acid, causing lactic acidosis. In addition, the production of cellular energy is diminished. The brain, which is especially dependent on this form of energy, is severely affected, resulting in the neurological problems associated with pyruvate dehydrogenase deficiency.

2.2. More About This Health Condition

Leigh syndrome

3. Other Names for This Gene

- ODPA_HUMAN
- PDHA
- PDHCE1A

- PDHE1-A type I
- PHE1A
- pyruvate dehydrogenase (lipoamide) alpha 1
- pyruvate dehydrogenase alpha 1
- pyruvate dehydrogenase complex, E1-alpha polypeptide 1
- pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial

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