GNE Gene

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Glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase genes

1. Introduction

The *GNE* gene provides instructions for making an enzyme that is found in cells and tissues throughout the body. This enzyme plays a key role in a chemical pathway that produces sialic acid, which is a simple sugar that attaches to the ends of more complex molecules on the surface of cells. By modifying these molecules, sialic acid influences a wide variety of cellular functions including cell movement (migration), attaching cells to one another (adhesion), signaling between cells, and inflammation.

The enzyme produced from the *GNE* gene is responsible for two steps in the formation of sialic acid. It first converts a molecule known as UDP-GlcNAc to a similar molecule called ManNAc. In the next step, the enzyme transfers a cluster of oxygen and phosphorus atoms (a phosphate group) to ManNAc to create ManNAc-6-phosphate. Other enzymes then convert ManNAc-6-phosphate to sialic acid.

2. Health Conditions Related to Genetic Changes

2.1. Inclusion Body Myopathy 2

More than 40 mutations in the *GNE* gene have been identified in people with inclusion body myopathy 2. Most of these mutations change single protein building blocks (amino acids) in several regions of the enzyme. A few mutations delete a piece of the enzyme or otherwise alter its structure.

Different *GNE* mutations cause inclusion body myopathy 2 in different populations. One mutation causes the disorder in people of Iranian Jewish heritage; this genetic change replaces the amino acid methionine with the amino acid threonine at position 712 in a region of the enzyme known as the kinase domain (written as Met712Thr or M712T). In the Japanese population, where the condition is called Nonaka myopathy, the most common *GNE* mutation replaces the amino acid valine with the amino acid leucine at position 572 in the enzyme's kinase domain (written as Val572Leu or V572L).

The mutations responsible for inclusion body myopathy 2 reduce the activity of the enzyme produced from the *GNE* gene, which decreases the production of sialic acid. As a result, less of this simple sugar is available to attach to cell surface molecules. Researchers are working to determine how a shortage of sialic acid leads to progressive muscle weakness in people with inclusion body myopathy 2. Sialic acid is important for the normal function of many different cells and tissues, so it is unclear why the signs and symptoms of this disorder appear to be limited to the skeletal muscles.

2.2. Sialuria

Several mutations in the *GNE* gene have been found to cause sialuria. Each of these mutations changes a single amino acid in a region of the enzyme known as the allosteric site. This region is critical for the normal regulation of the enzyme.

The enzyme produced from the *GNE* gene is carefully controlled to ensure that cells produce an appropriate amount of sialic acid. A feedback system shuts off the enzyme when no more sialic acid is needed. Mutations in the allosteric site disrupt this feedback mechanism, resulting in an overproduction of sialic acid. This simple sugar builds up within cells and is excreted in urine. Researchers are working to determine how an accumulation of sialic acid in the body interferes with normal development in people with sialuria.

3. Other Names for This Gene

- Bifunctional UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase
- DMRV
- GLCNE
- GLCNE_HUMAN
- IBM2
- N-acylmannosamine kinase
- Uae1
- UDP-GlcNAc-2-epimerase/ManAc kinase
- UDP-N-acetylglucosamine 2-epimerase/N-acetylmannosamine kinase

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