GJB1 Gene

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Gap junction protein beta 1

genes

1. Normal Function

The *GJB1* gene provides instructions for making a protein called connexin-32 (also known as gap junction beta 1). This protein is a member of the gap junction connexin family, which plays a role in cell communication by forming channels, or gap junctions, between cells. Gap junctions speed the transport of nutrients, charged particles (ions), and small molecules that carry communication signals between cells.

The connexin-32 protein is made in several tissues, including those of the liver, pancreas, kidney, and nervous system. In the nervous system, this protein is located in the cell membrane of specialized cells called Schwann cells and oligodendrocytes. Schwann cells are found in the peripheral nervous system, which consists of nerves connecting the brain and spinal cord (central nervous system) to muscles and sensory cells that detect sensations such as touch, pain, heat, and sound. Oligodendrocytes are located in the central nervous system.

Schwann cells and oligodendrocytes surround nerves and are involved in the production and long-term maintenance of a fatty substance called myelin. Myelin forms a protective coating (or sheath) around certain nerve cells that ensures the smooth and rapid transmission of nerve impulses.

The connexin-32 protein forms channels through the myelin sheath, allowing efficient transport and communication between the outer myelin layers and the interior of the Schwann cell or oligodendrocyte.

2. Health Conditions Related to Genetic Changes

2.1 Charcot-Marie-Tooth Disease

Researchers have identified more than 400 *GJB1* gene mutations in people with type X Charcot-Marie-Tooth disease, a disorder characterized by muscle weakness and sensory problems, especially in the hands and feet. A few of these mutations also cause hearing loss in individuals with this type of Charcot-Marie-Tooth disease.

Most *GJB1* gene mutations change single protein building blocks (amino acids) in the connexin-32 protein. It is unclear how these mutations lead to the characteristic features of Charcot-Marie-Tooth disease, including a loss of

myelin (demyelination) and the slowed transmission of nerve impulses in the peripheral nervous system. The altered protein may be broken down quickly or trapped inside the cell, preventing it from reaching the cell membrane to form gap junctions. In some cases, an altered protein reaches the cell membrane but does not form properly functioning gap junctions. The loss of functional gap junctions probably impairs the normal activities of Schwann cells, including myelin production. Malfunctioning gap junctions could also disrupt communication between Schwann cells and the underlying nerve cell, disturbing the transmission of nerve impulses.

In addition to the peripheral nervous system problems associated with this disorder, loss of myelin in the central nervous system has been reported in some people with Charcot-Marie-Tooth disease caused by *GJB1* gene mutations. These central nervous system abnormalities do not generally cause any symptoms. Research suggests that another connexin protein whose function overlaps with that of connexin-32 helps compensate for the mutated connexin-32 protein in the oligodendrocytes of the central nervous system.

3. Other Names for This Gene

- CMTX
- CMTX1
- connexin 32
- CX32
- CXB1_HUMAN
- gap junction protein, beta 1, 32kDa
- gap junction protein, beta 1, 32kDa (connexin 32, Charcot-Marie-Tooth neuropathy, X-linked)

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