SLC26A4 Gene

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solute carrier family 26 member 4

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1. Normal Function

The *SLC26A4* gene provides instructions for making a protein called pendrin. This protein transports negatively charged particles (ions), including chloride, iodide, and bicarbonate, across cell membranes. Pendrin is produced in several organs and tissues, particularly the inner ear and thyroid gland.

The thyroid gland is a butterfly-shaped organ at the base of the neck that releases hormones to help regulate growth and the rate of chemical reactions in the body (metabolism). In the thyroid, pendrin is believed to transport iodide ions out of certain cells. Iodide is needed for the normal production of thyroid hormones.

In the inner ear, pendrin likely helps control the proper balance of ions, including chloride and bicarbonate. Maintaining the proper levels of these ions appears to be particularly important during development of the inner ear, and it may influence the shape of bony structures such as the cochlea and vestibular aqueduct. The cochlea is a snail-shaped structure that helps process sound. The vestibular aqueduct is a bony canal that connects the inner ear with the inside of the skull.

Pendrin is also found in other tissues, including the kidneys, liver, and lining of the airways. Researchers are studying the role of pendrin's ion transport function in these tissues.

2. Health Conditions Related to Genetic Changes

2.1. Nonsyndromic hearing loss

Dozens of *SLC26A4* gene mutations have been identified in people with nonsyndromic hearing loss, which is loss of hearing that is not associated with signs and symptoms affecting other parts of the body. Mutations in this gene cause a form of nonsyndromic hearing loss called DFNB4. This form of hearing loss can either be present before a child learns to speak (prelingual) or begin after a child learns to speak (postlingual). Most people with DFNB4 also have an unusually large vestibular aqueduct (enlarged vestibular aqueduct, or EVA).

Mutations in the *SLC26A4* gene impair or eliminate the activity of pendrin, which upsets the balance of ions in the inner ear. These changes presumably affect the development of structures in the inner ear, including the cochlea and vestibular aqueduct. Studies suggest that the changes in ion levels also lead to the loss of sensory cells in the inner ear that are needed for hearing.

2.2. Pendred syndrome

Researchers have identified more than 150 mutations in the *SLC26A4* gene in people with Pendred syndrome. This condition is characterized by enlargement of the thyroid gland (called a goiter), hearing loss, and other abnormalities of the inner ear, including an enlarged vestibular aqueduct.

Some of the *SLC26A4* gene mutations change single protein building blocks (amino acids) used to make pendrin. Other mutations add or delete a small amount of DNA in the *SLC26A4* gene. All of these genetic changes impair or eliminate the activity of pendrin, which disrupts ion transport. In the thyroid, the disrupted ion transport prevents iodide ions from being available for thyroid hormone production. To compensate for the perceived lack of iodide, the thyroid tissue enlarges to form a goiter. In the inner ear, impaired pendrin activity alters the balance of ions, which presumably affects the development of structures including the cochlea and vestibular aqueduct. Studies suggest that the changes in ion levels also lead to the loss of sensory cells in the inner ear that are needed for hearing.

Because their signs and symptoms overlap, it can be difficult to distinguish Pendred syndrome from nonsyndromic hearing loss (DFNB4, described above). Many of the *SLC26A4* gene mutations associated with Pendred syndrome have also been found to cause DFNB4. Mutations in this gene can also cause other thyroid abnormalities; in a small number of people, *SLC26A4* gene mutations have been associated with an abnormally small thyroid gland (thyroid hypoplasia) that causes a loss of thyroid function from birth (congenital hypothyroidism). It is unclear whether Pendred syndrome, DFNB4, and thyroid hypoplasia caused by *SLC26A4* gene mutations are best considered as separate disorders or as a spectrum of related signs and symptoms.

3. Other Names for This Gene

- PDS
- pendrin
- S26A4_HUMAN
- solute carrier family 26 (anion exchanger), member 4
- solute carrier family 26, member 4

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