ABCC6 Gene

Subjects: Genetics & Heredity
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ATP binding cassette subfamily C member 6

genes

1. Normal Function

The *ABCC6* gene provides instructions for making a protein called multidrug resistance-associated protein 6 (MRP6, also known as the ABCC6 protein). This protein is found primarily in the liver and kidneys, with small amounts in other tissues such as the skin, stomach, blood vessels, and eyes. The MRP6 protein belongs to a group of proteins that transport molecules across cell membranes; however, little is known about the substances transported by MRP6.

Some studies suggest that MRP6 stimulates the release of a molecule called adenosine triphosphate (ATP) from cells through an unknown mechanism. This ATP is quickly broken down into other molecules called adenosine monophosphate (AMP) and pyrophosphate. Pyrophosphate helps control deposition of calcium (calcification) and other minerals (mineralization) in the body.

Other studies suggest that MRP6 transports a substance that is involved in the breakdown of ATP. This unidentified substance is thought to help prevent mineralization of tissues.

2. Health Conditions Related to Genetic Changes

2.1 Generalized arterial calcification of infancy

At least 13 mutations in the *ABCC6* gene have been identified in individuals with generalized arterial calcification of infancy (GACI), a life-threatening disorder characterized by abnormal calcification in the blood vessels that carry blood from the heart to the rest of the body (the arteries). Most of these mutations have also been identified in people with pseudoxanthoma elasticum (PXE), described below. These mutations lead to an absent or nonfunctional MRP6 protein. It is unclear how a lack of properly functioning MRP6 protein leads to GACI. This shortage may impair the release of ATP from cells. As a result, little pyrophosphate is produced and calcium accumulates in the blood vessels and other tissues affected by GACI. Alternatively, a lack of functioning MRP6 may impair the transport of a substance that would normally prevent mineralization, leading to the abnormal

accumulation of calcium characteristic of GACI. It is not known why the same mutations can cause GACI in some individuals and PXE in others.

2.2 Pseudoxanthoma elasticum

More than 200 *ABCC6* gene mutations that cause pseudoxanthoma elasticum (PXE) have been identified. PXE is a condition characterized by abnormal accumulation of calcium and other minerals in elastic fibers, a component of connective tissues that provide strength and flexibility to structures throughout the body. The *ABCC6* gene mutations involved in this condition lead to an absence of MRP6 protein or an altered protein that does not function properly. The most common mutation in the United States, found in about 28 percent of people with PXE, deletes part of the *ABCC6* gene. (This mutation is written as Ex23_29del.)

It is unclear how loss of MRP6 function leads to PXE. As in GACI (described above), this loss may impair the release of ATP or the transport of a substance that normally prevents mineralization. Without MRP6 function, calcium and other minerals accumulate in elastic fibers of the skin, eyes, blood vessels and other tissues affected by PXE.

3. Other Names for This Gene

- ABC34
- anthracycline resistance-associated protein
- ARA
- ATP-binding cassette, sub-family C (CFTR/MRP), member 6
- EST349056
- MLP1
- MOAT-E
- MRP6
- MRP6_HUMAN
- multidrug resistance-associated protein 6
- multispecific organic anion transporter-E

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