RNF213 Gene

Subjects: Genetics & Heredity
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ring finger protein 213

genes

1. Normal Function

The *RNF213* gene provides instructions for making a protein whose role is unknown. The RNF213 protein, which is found in tissues throughout the body, contains specific regions (domains) that hint at possible functions. One domain, known as a RING finger, is found in proteins that have an enzyme activity known as E3 ubiquitin-protein ligase. Proteins with this activity target other proteins to be broken down (degraded) within cells. Protein degradation is a normal process that removes damaged or unnecessary proteins and helps maintain the normal functions of cells. Proteins with a RING finger domain are involved in many different cellular functions, including cell growth and division, the transmission of chemical signals (signal transduction), and the self-destruction of cells (apoptosis).

The RNF213 protein also contains two regions called AAA+ ATPase domains. Proteins with these domains typically regulate mechanical processes in the cell, such as protein unfolding, DNA unwinding, or transporting molecules.

Although the function of the RNF213 protein is unknown, studies suggest that it plays a role in the proper development of blood vessels.

2. Health Conditions Related to Genetic Changes

2.1. Moyamoya disease

At least 24 genetic changes in the *RNF213* gene have been associated with moyamoya disease. This condition is characterized by narrowing of blood vessels in the brain and subsequent growth of networks of small, fragile blood vessels. The resulting lack of blood flow in the brain leads to strokes and other features of the condition.

Changes in the *RNF213* gene involved in moyamoya disease replace single protein building blocks (amino acids) in the RNF213 protein. The most common change is a normal variation (polymorphism) of the gene that replaces the amino acid arginine with the amino acid lysine at protein position 4810 (written as Arg4810Lys or R4810K). This genetic change is found in a majority of affected individuals in Asian populations and is relatively common in

unaffected individuals in these populations, occurring in about 1 percent. (This phenomenon, in which people with an altered copy of the gene never develop the condition, is known as reduced penetrance.) However, the Arg4810Lys change is not found in affected individuals of European descent. These individuals have rarer *RNF213* gene mutations that change single amino acids in the protein.

Little is known about the effect of these changes on the function of the RNF213 protein, and researchers are unsure how the changes contribute to the characteristic blood vessel abnormalities of moyamoya disease. It is unclear if *RNF213* gene mutations are involved in the narrowing of blood vessels in the brain. For unknown reasons, people with moyamoya disease have elevated levels of proteins involved in cell and tissue growth, including the growth of blood vessels (angiogenesis). An excess of these proteins could account for the growth of new blood vessels characteristic of moyamoya disease. It is not clear if changes in the *RNF213* gene are involved in the overproduction of these proteins.

Little is known about the cause of moyamoya disease. Studies suggest that other genes could be involved in development of the condition. It has been suggested that other factors, such as infection or inflammation, in combination with genetic changes may be necessary for development of moyamoya disease.

3. Other Names for This Gene

- ALK lymphoma oligomerization partner on chromosome 17
- ALO17
- C17orf27
- E3 ubiquitin-protein ligase RNF213
- KIAA1554
- KIAA1618
- MYMY2
- mysterin
- MYSTR
- NET57
- RN213_HUMAN

References

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