FAT4 Gene

Subjects: Genetics & Heredity
Contributor: Vivi Li

FAT atypical cadherin 4

Keywords: genes

1. Normal Function

The *FAT4* gene provides instructions for making a protein that is found in most tissues. The protein spans the membrane surrounding cells so that part of the protein is outside the cell and part of the protein is inside the cell. The precise function of the FAT4 protein is largely unknown; however, research shows that the FAT4 protein is likely involved in determining the position of various components within cells (cell polarity). The FAT4 protein is also thought to function as a tumor suppressor, which means that it keeps cells from growing and dividing too rapidly or in an uncontrolled way.

2. Health Conditions Related to Genetic Changes

2.1 Hennekam Syndrome

At least seven mutations in the *FAT4* gene have been found to cause Hennekam syndrome, an inherited disorder resulting from malformation of the lymphatic system, which consists of a network of vessels that transport lymph fluid and immune cells throughout the body. The *FAT4* gene mutations that cause Hennekam syndrome reduce the activity of the FAT4 protein, which seems to impair normal development of the lymphatic system. However, the mechanism is unknown. A poorly formed lymphatic system leads to lymphatic vessels that are abnormally expanded (lymphangiectasia) and are prone to break open (rupture), puffiness or swelling caused by a buildup of fluid (lymphedema), and other features of Hennekam syndrome. *FAT4* gene mutations account for about 25 percent of all cases of Hennekam syndrome.

2.2 Other Disorders

Mutations in the *FAT4* gene have also been found in individuals who have van Maldergem syndrome, a condition characterized by intellectual disability, hearing loss, skeletal abnormalities, and a brain malformation called periventricular heterotopia. The *FAT4* gene mutations that cause van Maldergem syndrome lead to a decrease in FAT4 protein function. It is thought that a decrease in FAT4 protein activity in the brain disrupts the polarity of nerve cells in the brain, which leads to periventricular heterotopia.

It is unknown how mutations in the *FAT4* gene can cause the signs and symptoms of van Maldergem syndrome in some people but lead to different signs and symptoms in those with Hennekam syndrome (described above). One mutation that replaces the protein building block (amino acid) glutamic acid with the amino acid lysine at position 2375 in the FAT4 protein (written as Glu2375Lys or E2375K) has been found in both individuals with van Maldergem syndrome and those with Hennekam syndrome.

FAT4 gene mutations have also been found in many types of cancers, including a type of skin cancer called head and neck squamous cell carcinoma, an aggressive form of skin cancer called melanoma, a liver cancer called hepatocellular carcinoma, stomach (gastric) cancer, and pancreatic cancer. The *FAT4* gene mutations involved in these cancers are different from the ones that cause van Maldergem syndrome and Hennekam syndrome (described above). The *FAT4* gene mutations associated with cancers are called somatic mutations; they are found only in cells that become cancerous and are not inherited. It is likely that these mutations prevent the FAT4 protein from acting as a tumor suppressor, contributing to the uncontrollable growth and division of cells that is characteristic of cancer. People with van Maldergem syndrome and Hennekam syndrome are not thought to have an increased risk of developing cancer.

3. Other Names for This Gene

- cadherin family member 14
- cadherin-related family member 11
- CDHF14
- CDHR11
- FAT tumor suppressor homolog 4
- FAT-J
- fat-like cadherin protein FAT-J
- FAT4_HUMAN
- FATJ
- NBLA00548
- protocadherin Fat 4
- VMLDS2

References

1. Alders M, Al-Gazali L, Cordeiro I, Dallapiccola B, Garavelli L, Tuysuz B,Salehi F, Haagmans MA, Mook OR, Majoie CB, Mannens MM, Hennekam RC. Hennekamsyndrome can be caused by FAT4 mutations and be allelic to Van Maldergemsyndrome. Hum Genet. 2014 Sep;133(9):1161-7. doi: 10.1007/s00439-014-1456-y.
2. Katoh M. Function and cancer genomics of FAT family genes (review). Int JOncol. 2012 Dec;41(6):1913-8. doi: 10.3892/ijo.2012.1669.Review.
3. Katoh Y, Katoh M. Comparative integromics on FAT1, FAT2, FAT3 and FAT4. Int J Mol Med. 2006 Sep;18(3):523-8.