FAT4 gene
FAT atypical cadherin 4

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.

Health Conditions Related to Genetic Changes
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.

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.

**Chromosomal Location**

Cytogenetic Location: 4q28.1, which is the long (q) arm of chromosome 4 at position 28.1

Molecular Location: base pairs 125,314,913 to 125,492,932 on chromosome 4 (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

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

Additional Information & Resources

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28FAT4%5BTIAB%5D%29+OR+%28FAT+atypical+cadherin+4%5BTIAB%5D%29%29+AND+%28%28Genes%5B MH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english %5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM
• FAT TUMOR SUPPRESSOR, DROSOPHILA, HOMOLOG OF, 4
  http://omim.org/entry/612411

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_FAT4.html
• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=FAT4%5Bgene%5D
• HGNC Gene Symbol Report
• Monarch Initiative
• NCBI Gene
• UniProt
  https://www.uniprot.org/uniprot/Q6V0I7

Sources for This Summary
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24913602
• OMIM: FAT TUMOR SUPPRESSOR, DROSOPHILA, HOMOLOG OF, 4
  http://omim.org/entry/612411


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