ETV6 gene
ETS variant 6

Normal Function

The ETV6 gene provides instructions for producing a protein that functions as a transcription factor, which means that it attaches (binds) to specific regions of DNA and controls the activity of certain genes. The ETV6 protein is found in the nucleus of cells throughout the body, where it turns off (represses) gene activity. It plays a key role in development before birth and in regulating blood cell formation.

Health Conditions Related to Genetic Changes

**PDGFRB-associated chronic eosinophilic leukemia**

PDGFRB-associated chronic eosinophilic leukemia, a type of cancer of blood-forming cells, can be caused by a genetic rearrangement known as a translocation that brings together part of the ETV6 gene and part of another gene called PDGFRB, creating the ETV6-PDGFRB fusion gene. The translocation that leads to the ETV6-PDGFRB fusion gene is a somatic mutation, which is acquired during a person's lifetime and occurs initially in a single cell. This cell continues to grow and divide, producing a group of cells with the same mutation (a clonal population).

The protein produced from the ETV6-PDGFRB fusion gene, called ETV6/PDGFRβ, functions differently than the proteins normally produced from the individual genes. Unlike the normal PDGFRβ protein, the fusion protein is always active, which means certain cell signaling pathways are constantly turned on. The fusion protein is unable to repress gene activity regulated by the normal ETV6 protein, so gene activity is increased. The overactive signaling pathways and abnormal gene activity increase the proliferation and survival of cells. When the ETV6-PDGFRB fusion gene mutation occurs in cells that develop into blood cells, the growth of white blood cells called eosinophils (and occasionally other white blood cells, such as neutrophils and mast cells) is poorly controlled, leading to PDGFRB-associated chronic eosinophilic leukemia. It is unclear why eosinophils are preferentially affected by this genetic change.

**Other cancers**

Translocations involving the ETV6 gene and more than 30 other genes have been found to cause different types of leukemia, including acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL), and a bone marrow disease called myelodysplastic syndrome (MDS). Depending on the gene fused with ETV6, a number of mechanisms can cause these conditions, such as impaired regulation of
gene activity, abnormal signaling, or loss of normal gene function. The \textit{ETV6} gene
translocations that cause these diseases are somatic mutations and are not inherited.

\textbf{Chromosomal Location}

Cytogenetic Location: 12p13.2, which is the short (p) arm of chromosome 12 at position
13.2

Molecular Location: base pairs 11,649,601 to 11,895,402 on chromosome 12 (\textit{Homo
sapiens Updated Annotation Release 109.20190607, GRCh38.p13}) (\textit{NCBI})

\textbf{Other Names for This Gene}

- ETS-related protein Tel1
- ETS translocation variant 6
- ets variant 6
- ets variant gene 6 (TEL oncogene)
- ETV6\_HUMAN
- TEL
- TEL1 oncogene
- transcription factor ETV6

\textbf{Additional Information & Resources}

\textbf{Educational Resources}

  https://www.ncbi.nlm.nih.gov/books/NBK12538/#A1403
  https://www.ncbi.nlm.nih.gov/books/NBK13714/#A1394
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ETV6%5BTIAB%5D%29+OR+%28TEL%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ETS VARIANT GENE 6
  http://omim.org/entry/600618
- LEUKEMIA, ACUTE MYELOID
  http://omim.org/entry/601626

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/ETV6ID38.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ETV6%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:2120
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P41212

Sources for This Summary

- OMIM: ETS VARIANT GENE 6
  http://omim.org/entry/600618
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22162288
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22823977
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Reviewed: February 2013
Published: June 25, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services