YWHAE gene
tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein epsilon

Normal Function

The YWHAE gene provides instructions for making the 14-3-3 epsilon (ε) protein, which is part of the large 14-3-3 protein family. Proteins in this family attach (bind) to other proteins involved in cell signaling. 14-3-3 proteins either turn on (activate) or turn off (inactivate) these other proteins. The 14-3-3ε protein helps to regulate a variety of processes including cell division and sensitivity to insulin, a hormone that helps control blood sugar levels.

The 14-3-3ε protein is active in tissues throughout the body, although its function is sometimes unclear. In the brain, this protein is involved in directing the movement of nerve cells (neuronal migration) by binding to other proteins involved in this process. It is thought that the 14-3-3ε protein is critical for proper neuronal migration and normal brain development.

Health Conditions Related to Genetic Changes

Miller-Dieker syndrome

The characteristic signs and symptoms of Miller-Dieker syndrome are caused by a deletion of genetic material near the end of the short (p) arm of chromosome 17. The chromosomal region that is typically deleted contains multiple genes, including the YWHAE gene. As a result of the deletion, people with this condition have only one copy of the YWHAE gene in each cell instead of the usual two copies.

A deletion of one copy of the YWHAE gene in each cell reduces the amount of 14-3-3ε protein by about half. A shortage of 14-3-3ε protein increases the severity of lissencephaly (a problem with brain development in which the surface of the brain is abnormally smooth) in people with Miller-Dieker syndrome.

Schizophrenia

Other disorders

A deletion that only involves the YWHAE gene can also cause health problems. People with a YWHAE gene deletion are missing one copy of the gene in each cell, which reduces the amount of 14-3-3ε protein that is produced by about half. A deficiency (shortage) of this protein is thought to cause short stature; intellectual disability; and distinctive facial features including a prominent forehead, wide
nasal bridge, and small jaw. People with a \textit{YWHAE} gene deletion do not have lissencephaly but tend to have other brain abnormalities.

**Chromosomal Location**

Cytogenetic Location: \textit{17p13.3}, which is the short (p) arm of chromosome 17 at position 13.3

Molecular Location: base pairs 1,344,275 to 1,400,262 on chromosome 17 (\textit{Homo sapiens\textsuperscript{Updated Annotation Release 109.20200522, GRCh38.p13}}) (\textit{NCBI})

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

- 14-3-3 epsilon
- 14-3-3E
- 1433E\_HUMAN
- KCIP-1
- mitochondrial import stimulation factor L subunit
- protein kinase C inhibitor protein-1
- tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon
- tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide
- tyrosine 3/tryptophan 5-monooxygenase activation protein, epsilon polypeptide

**Additional Information & Resources**

**Educational Resources**

- Madame Curie Bioscience Database: 14-3-3 Proteins
  https://www.ncbi.nlm.nih.gov/books/NBK5962/#A10508
  https://www.ncbi.nlm.nih.gov/books/NBK10831/
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28YWHAE%5BTIAB%5D%29+OR+%28%2814-3-3E%5BTIAB%5D%29%29+AND+%22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- TYROSINE 3-MONOOXYGENASE/TRYPTOPHAN 5-MONOOXYGENASE ACTIVATION PROTEIN, EPSILON ISOFORM
  http://omim.org/entry/605066

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_YWHAE.html
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:7531
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P62258

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8684458
  Deletion of YWHAE in a patient with periventricular heterotopias and pronounced corpus callosum hypoplasia.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19635726
  Microdeletions including YWHAE in the Miller-Dieker syndrome region on chromosome 17p13.3 result in facial dysmorphisms, growth restriction, and cognitive impairment.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19584063
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9312143

• OMIM: TYROSINE 3-MONOOXYGENASE/TRYPTOPHAN 5-MONOOXYGENASE ACTIVATION PROTEIN, EPSILON ISOFORM
  http://omim.org/entry/605066

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17728103

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12796778

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