DEPDC5 gene
DEP domain containing 5

Normal Function

The **DEPDC5** gene provides instructions for making a protein that is one piece of a group of proteins (complex) called GATOR1. This complex is found in cells throughout the body, where it regulates a signaling pathway called the mTOR pathway. The mTOR pathway is involved in cell growth and division (proliferation), the survival of cells, and the creation (synthesis) of new proteins. The role of the GATOR1 complex is to block this pathway by inhibiting (stopping) the activity of a complex called mTOR complex 1 (mTORC1) that is integral to the mTOR pathway.

In the brain, the mTOR pathway regulates many processes, including the growth and development of nerve cells and their ability to change and adapt over time (plasticity).

Health Conditions Related to Genetic Changes

**Familial focal epilepsy with variable foci**

More than 80 mutations in the **DEPDC5** gene have been found to cause familial focal epilepsy with variable foci (FFEVF), which is an uncommon form of recurrent seizures (epilepsy) that runs in families. Affected individuals experience focal seizures, which are seizures that do not cause a loss of consciousness. Most of the **DEPDC5** gene mutations lead to the production of an abnormally short protein that is quickly broken down. As a result, formation of normal GATOR1 complex is reduced, leading to overactivity of mTORC1 and excessive signaling of the mTOR pathway. It is not clear how an abnormally active mTOR pathway leads to the focal seizures of FFEVF. Research suggests that increased mTOR pathway signaling in the brain leads to changes in the connections between nerve cells (synapses) and increased activation (excitation) of nerve cells, which can cause seizures.

For unknown reasons, some people with FFEVF caused by a **DEPDC5** gene mutation never develop the condition, a situation known as reduced penetrance. It is estimated that 60 percent of individuals with **DEPDC5** gene mutations go on to develop FFEVF.

**Other disorders**

Mutations in the **DEPDC5** gene can cause other seizure disorders, known as familial mesial temporal lobe epilepsy and infantile spasms. Similar to individuals with FFEVF (described above), people with familial mesial temporal lobe epilepsy have focal seizures. They may also have feelings of déjà vu, fear, or nausea during the seizure.
Infantile spasms are seizures that usually appear before the age of 1 and involve recurrent muscle contractions.

As in FFEVF, most of the \textit{DEPDC5} gene mutations that cause familial mesial temporal lobe epilepsy or infantile spasms lead to reduced GATOR1 complex formation and an abnormally active mTOR pathway. It is unclear why individuals with mutations in the same gene develop different seizure disorders.

\textbf{Chromosomal Location}

Cytogenetic Location: 22q12.2-q12.3, which is the long (q) arm of chromosome 22 between positions 12.2 and 12.3

Molecular Location: base pairs 31,753,968 to 31,908,033 on chromosome 22 (Homo sapiens Updated Annotation Release 109.20200228, GRCh38.p13) (NCBI)

\begin{center}
\includegraphics[width=\textwidth]{chromosome.png}
\end{center}

Credit: Genome Decoration Page/NCBI

\textbf{Other Names for This Gene}

- DEP.5
- FFEVF
- FFEVF1
- KIAA0645

\textbf{Additional Information & Resources}

\textbf{Educational Resources}

- Jasper's Basic Mechanisms of the Epilepsies (fourth edition, 2012): mTOR and Epileptogenesis in Developmental Brain Malformations
  https://www.ncbi.nlm.nih.gov/books/NBK98145/

\textbf{Clinical Information from GeneReviews}

- DEPDC5-Related Epilepsy
  https://www.ncbi.nlm.nih.gov/books/NBK385626
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28DEPDC5%5BTIAB%5D%29+OR+%28DEP+domain+containing+5%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- DEP DOMAIN-CONTAINING PROTEIN 5
  http://omim.org/entry/614191

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_DEPDC5.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=DEPDC5%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:9681
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/O75140

Sources for This Summary

• OMIM: DEP DOMAIN-CONTAINING PROTEIN 5
  http://omim.org/entry/614191

• Dibbens LM, de Vries B, Donatello S, Heron SE, Hodgson BL, Chintawar S, Crompton DE, Hughes
  JN, Bellows ST, Klein KM, Callenbach PM, Corbett MA, Gardner AE, Kivity S, Iona X, Regan BM,
  Cossette P, Thomas PQ, Gecz J, Brouwer OF, Andermann F, Andermann E, van den
  Maagdenberg AM, Pandolfo M, Berkovic SF, Scheffer IE. Mutations in DEPDC5 cause familial focal
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23542697

  Marescaux C, Miles R, Baulac M, Hirsch E, Leguern E, Baulac S. Mutations of DEPDC5 cause
  Epub 2013 Mar 31.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23542701
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5010101/

• Scheffer IE, Heron SE, Regan BM, Mandelstam S, Crompton DE, Hodgson BL, Licchetta L, Provini
  Mutations in mammalian target of rapamycin regulator DEPDC5 cause focal epilepsy with brain
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24585383

• Weckhuysen S, Marsan E, Lambrecq V, Marchal C, Morin-Brureau M, An-Gourfinkel I, Baulac M,
  Leguern E, Picard F, Baulac S. Involvement of GATOR complex genes in familial focal epilepsies
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27173016

• van Kranenburg M, Hoogeveen-Westerveld M, Nellist M. Preliminary functional assessment and
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25366275

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