FZD4 gene
frizzled class receptor 4

Normal Function

The FZD4 gene provides instructions for making a protein called frizzled-4. This protein is embedded in the outer membrane of many types of cells, where it is involved in transmitting chemical signals from outside the cell to the cell's nucleus. Specifically, frizzled-4 participates in the Wnt signaling pathway, a series of steps that affect the way cells and tissues develop. Wnt signaling is important for cell division (proliferation), attachment of cells to one another (adhesion), cell movement (migration), and many other cellular activities.

Studies suggest that, at the cell surface, the frizzled-4 protein interacts with a protein called norrin (produced from the NDP gene). The two proteins fit together like a key in a lock. Researchers suspect that when norrin attaches (binds) to frizzled-4, it initiates a multi-step process that regulates the activity of certain genes. During early development, signaling by norrin and frizzled-4 plays a critical role in the specialization of cells in the retina, which is the light-sensing tissue at the back of the eye. This signaling pathway is also involved in the establishment of a blood supply to the retina and the inner ear.

Health Conditions Related to Genetic Changes

Familial exudative vitreoretinopathy

More than 20 mutations in the FZD4 gene have been identified in people with an eye disorder called familial exudative vitreoretinopathy. Some of these mutations change single protein building blocks (amino acids) in frizzled-4, while others insert or delete genetic material in the FZD4 gene. Most FZD4 mutations reduce the amount of frizzled-4 that is produced within cells. Other mutations are thought to result in the production of an unstable protein that cannot bind to norrin.

A reduction in the amount of frizzled-4 disrupts chemical signaling in the developing eye, which interferes with the formation of blood vessels at the edges of the retina. The resulting abnormal blood supply to this tissue leads to retinal damage and vision loss in some people with familial exudative vitreoretinopathy.
**Chromosomal Location**

Cytogenetic Location: 11q14.2, which is the long (q) arm of chromosome 11 at position 14.2

Molecular Location: base pairs 86,945,679 to 86,955,395 on chromosome 11 (Homo sapiens Updated Annotation Release 109.20200228, GRCh38.p13) (NCBI)

[Diagram of chromosome 11 with highlighted region]

**Credit:** Genome Decoration Page/NCBI

**Other Names for This Gene**

- CD344
- EVR1
- FEVR
- frizzled 4
- frizzled family receptor 4
- frizzled homolog 4 (Drosophila)
- Fz-4
- FZD4_HUMAN
- FZD4S
- FzE4
- GPCR
- MGC34390
- WNT receptor frizzled-4

**Additional Information & Resources**

**Educational Resources**

- Developmental Biology (sixth edition, 2000): The Wnt signal transduction pathway (figure)
  https://www.ncbi.nlm.nih.gov/books/NBK10043/?rendertype=figure&id=A1062
Clinical Information from GeneReviews

- Familial Exudative Vitreoretinopathy, Autosomal Dominant
  https://www.ncbi.nlm.nih.gov/books/NBK1147

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28FZD4%5BTIAB%5D%29+OR+%28frizzled+4%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- FRIZZLED CLASS RECEPTOR 4
  http://omim.org/entry/604579

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/FZD4ID40655ch11q14.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=FZD4%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:8322
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/Q9ULV1

Sources for This Summary

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  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1920788/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17093393
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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15223780

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15035989

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