PDGFRB gene
platelet derived growth factor receptor beta

Normal Function

The PDGFRB gene provides instructions for making a protein called platelet-derived growth factor receptor beta (PDGFRβ), which is part of a family of proteins called receptor tyrosine kinases. Receptor tyrosine kinases transmit signals from the cell surface into the cell through a process called signal transduction. The PDGFRβ protein is found in the cell membrane of certain cell types, where a protein called platelet-derived growth factor attaches (binds) to it. This binding turns on (activates) the PDGFRβ protein, which then activates other proteins inside the cell by adding a cluster of oxygen and phosphorus atoms (a phosphate group) at specific positions. This process, called phosphorylation, leads to the activation of a series of proteins in multiple signaling pathways.

The signaling pathways stimulated by the PDGFRβ protein control many important processes in the cell such as growth and division (proliferation), movement, and survival. PDGFRβ protein signaling is important for the development of many types of cells throughout the body.

Health Conditions Related to Genetic Changes

PDGFRB-associated chronic eosinophilic leukemia

Genetic rearrangements (translocations) involving the PDGFRB gene cause a type of cancer of blood-forming cells called PDGFRB-associated chronic eosinophilic leukemia. This condition is characterized by an increased number of eosinophils, a type of white blood cell. The most common of these translocations brings together part of the PDGFRB gene with another gene called ETV6, whose function is to turn off gene activity. Together, these pieces create the ETV6-PDGFRB fusion gene. Occasionally, genes other than ETV6 are fused with the PDGFRB gene. The translocations that lead to these fusion genes are somatic mutations, which are acquired during a person's lifetime and occur 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 (as well as other PDGFRB fusion genes) functions differently than the proteins normally produced from the individual genes. The ETV6/PDGFRβ fusion protein does not require ligand binding to be activated and cannot bind to DNA to turn off gene activity. As a result,
signaling pathways are constantly turned on (constitutively activated) and gene activity is increased, which increases the proliferation and survival of cells.

When the *ETV6-PDGFRB* fusion gene mutation occurs in cells that develop into blood cells, the growth of 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.

**Primary familial brain calcification**

At least six mutations in the *PDGFRB* gene have been found to cause primary familial brain calcification. This condition is characterized by abnormal deposits of calcium (calcification) in the brain, which can lead to movement and psychiatric problems. These mutations change single protein building blocks (amino acids) in the PDGFRβ protein. These changes impair the protein’s signaling ability.

It is unclear how *PDGFRB* gene mutations cause primary familial brain calcification. The altered signaling may result in an abnormally large amount of calcium entering the cells that line blood vessels in the brain, leading to calcification of these blood vessels. Alternatively, changes in PDGFRB signaling could disrupt processes that regulate levels of phosphate and calcium in brain cells, leading to the formation of calcium deposits. In the brain, the excess phosphate combines with calcium and forms deposits.

The *PDGFRB* gene is active (expressed) throughout the body; it is unclear why the effects of these mutations are limited to structures deep within the brain that help start and control movement (basal ganglia) and to other brain regions that are involved in primary familial brain calcification.

**Other disorders**

Additional mutations in the *PDGFRB* gene cause a variety of disorders including infantile myofibromatosis; Kosaki overgrowth syndrome; and premature aging syndrome, Penttinen type.

Infantile myofibromatosis is a muscle disorder that causes the formation of multiple noncancerous (benign) tumors in the skin, muscles, or bones. These tumors are generally present at birth or in early infancy.

Kosaki overgrowth syndrome is characterized by above-average height and large hands and feet. Affected individuals have highly stretchy (elastic) and fragile skin. People with this condition also have distinctive facial features and brain abnormalities that result in intellectual disability and psychological problems.

Premature aging syndrome, Penttinen type is characterized by a lack of fatty tissue under the skin (lipoatrophy). This lack of fat, together with thin, wrinkled skin and veins visible beneath the skin, makes affected individuals look older than their biological age.
In all of these conditions, **PDGFRB** gene mutations result in increased cell signaling. While it is unclear how mutations in one gene can lead to so many different conditions, it is thought that particular mutations may affect different signaling pathways, leading to changes in specific body systems.

**Chromosomal Location**

Cytogenetic Location: 5q32, which is the long (q) arm of chromosome 5 at position 32

Molecular Location: base pairs 150,113,839 to 150,155,845 on chromosome 5 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Other Names for This Gene

- beta-type platelet-derived growth factor receptor
- CD140 antigen-like family member B
- CD140B
- PDGF-R-beta
- PDGFR-1
- PDGFR-beta
- PDGFR1
- PGFRB_HUMAN
- platelet-derived growth factor receptor 1
- platelet-derived growth factor receptor beta
- platelet-derived growth factor receptor, beta polypeptide
Additional Information & Resources

Educational Resources

• Holland-Frei Cancer Medicine (sixth edition, 2003): Chromosomal Rearrangements
  https://www.ncbi.nlm.nih.gov/books/NBK12538/#A1403

• Holland-Frei Cancer Medicine (sixth edition, 2003): Growth Factor Receptors
  https://www.ncbi.nlm.nih.gov/books/NBK13714/#A1392

• Holland-Frei Cancer Medicine (sixth edition, 2003): PDGFRB as a Therapeutic Target
  https://www.ncbi.nlm.nih.gov/books/NBK12453/#A13684

Clinical Information from GeneReviews

• Primary Familial Brain Calcification
  https://www.ncbi.nlm.nih.gov/books/NBK1421

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28PDGFRB%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• KOSAKI OVERGROWTH SYNDROME
  http://omim.org/entry/616592

• MYOFIBROMATOSIS, INFANTILE, 1
  http://omim.org/entry/228550

• PLATELET-DERIVED GROWTH FACTOR RECEPTOR, BETA
  http://omim.org/entry/173410

• PREMATURE AGING SYNDROME, PENTTINEN TYPE
  http://omim.org/entry/601812

Research Resources

• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/PDGFRBID21ch5q32.html

• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PDGFRB%5Bgene%5D

• HGNC Gene Symbol Report

• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5159
Sources for This Summary


- OMIM: KOSAKI OVERGROWTH SYNDROME http://omim.org/entry/616592

- OMIM: MYOFIBROMATOSIS, INFANTILE, 1 http://omim.org/entry/228550


- OMIM: PLATELET-DERIVED GROWTH FACTOR RECEPTOR, BETA http://omim.org/entry/173410

- OMIM: PREMATURE AGING SYNDROME, PENTTINEN TYPE http://omim.org/entry/601812


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