

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 (PDGFR β), 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 PDGFR β 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 PDGFR β 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 PDGFR β protein control many important processes in the cell such as growth and division (proliferation), movement, and survival. PDGFR β 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/PDGFR β 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 PDGFR β 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.

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

Tests Listed in the Genetic Testing Registry

- Tests of PDGFRB ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5159\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5159[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?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

- PREMATURE AGING SYNDROME, PENTTINEN TYPE; PENTT (<https://omim.org/entry/601812>)
- PLATELET-DERIVED GROWTH FACTOR RECEPTOR, BETA; PDGFRB (<https://omim.org/entry/173410>)
- MYOFIBROMATOSIS, INFANTILE, 1; IMF1 (<https://omim.org/entry/228550>)
- KOSAKI OVERGROWTH SYNDROME; KOGS (<https://omim.org/entry/616592>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/5159>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=PDGFRB\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=PDGFRB[gene]))

References

- Apperley JF, Gardembas M, Melo JV, Russell-Jones R, Bain BJ, Baxter EJ, Chase A, Chessells JM, Colombat M, Dearden CE, Dimitrijevic S, Mahon FX, Marin D, Nikolova Z, Olavarria E, Silberman S, Schultheis B, Cross NC, Goldman JM. Response to imatinib mesylate in patients with chronic myeloproliferative diseases with rearrangements of the platelet-derived growth factor receptor beta. *N Engl J Med*. 2002 Aug 15;347(7):481-7. doi: 10.1056/NEJMoa020150. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12181402>)
- Arefi M, Garcia JL, Penarrubia MJ, Queizan JA, Hermosin L, Lopez-Corral L, Megido M, Giraldo P, de las Heras N, Vanegas RJ, Gutierrez NC, Hernandez-Rivas JM. Incidence and clinical characteristics of myeloproliferative neoplasms displaying a PDGFRB rearrangement. *Eur J Haematol*. 2012 Jul;89(1):37-41. doi:10.1111/j.1600-0609.2012.01799.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22587685>)
- Bain BJ. Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB or FGFR1. *Haematologica*. 2010 May;95(5):696-8. doi:10.3324/haematol.2009.021675. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20442440>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2864371/>)
- Cross NC, Reiter A. Fibroblast growth factor receptor and platelet-derived growth factor receptor abnormalities in eosinophilic myeloproliferative disorders. *Acta Haematol*. 2008;119(4):199-206. doi: 10.1159/000140631. Epub 2008 Jun 20. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18566537>)
- Nicolas G, Pottier C, Maltete D, Coutant S, Rovelet-Lecrux A, Legallic S, Rousseau S, Vaschalde Y, Guyant-Marechal L, Augustin J, Martinaud O, Defebvre L, Krystkowiak P, Pariente J, Clanet M, Labauge P, Ayrignac X, Lefaucheur R, Le Berl, Frebourg T, Hannequin D, Campion D. Mutation of the PDGFRB gene as a cause of idiopathic basal ganglia calcification. *Neurology*. 2013 Jan 8;80(2):181-7. doi:10.1212/WNL.0b013e31827ccf34. Epub 2012 Dec 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23255827>)

Genomic Location

The *PDGFRB* gene is found on chromosome 5 (<https://medlineplus.gov/genetics/chromosome/5/>).

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