**PDGFRA gene**

platelet derived growth factor receptor alpha

**Normal Function**

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

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

**Health Conditions Related to Genetic Changes**

**PDGFRA-associated chronic eosinophilic leukemia**

Genetic abnormalities that involve the *PDGFRA* gene cause a type of blood cell cancer called *PDGFRA*-associated chronic eosinophilic leukemia. This condition is characterized by an increased number of eosinophils, a type of white blood cell involved in allergic reactions. These genetic abnormalities are somatic mutations, which are mutations acquired during a person's lifetime that are present only in certain cells. The most common of these genetic abnormalities is a deletion of genetic material from chromosome 4 that brings together parts of two genes, *FIP1L1* and *PDGFRA*, creating the *FIP1L1-PDGFRA* fusion gene. Occasionally, genes other than *FIP1L1* are fused with the *PDGFRA* gene. Mutations that change single DNA building blocks in the *PDGFRA* gene (point mutations) can also cause this condition, although these mutations are seen very rarely.

The protein produced from the *FIP1L1-PDGFRA* fusion gene (as well as other *PDGFRA* fusion genes) has the function of the PDGFRA protein. However, unlike the normal PDGFRA protein, the fusion protein does not require binding of the platelet-derived growth factor protein to be activated. Similarly, point mutations in the *PDGFRA* gene can result in a PDGFRA protein that is activated without ligand binding. As a result, the signaling pathways are constantly turned on (constitutively...
activated), which increases the proliferation and survival of cells. When the FIP1L1-
PDGFRA fusion gene mutation or point mutations in the PDGFRA gene occur in early
blood cells, the growth of eosinophils (and occasionally other blood cells) is poorly
controlled, leading to PDGFRA-associated chronic eosinophilic leukemia. It is unclear
why eosinophils are preferentially affected by this genetic change.

Gastrointestinal stromal tumor

Mutations in the PDGFRA gene are associated with gastrointestinal stromal tumors
(GISTs). GISTs are a type of tumor that occurs in the gastrointestinal tract, most
commonly in the stomach or small intestine. The majority of GISTs associated with
a mutation in the PDGFRA gene occur in the stomach. In most cases, the genetic
changes are acquired during a person's lifetime and are called somatic mutations.
Somatic mutations, which lead to sporadic GISTs, are present only in the tumor
cells and are not inherited. Less commonly, PDGFRA gene mutations that increase
the risk of developing GISTs are inherited from a parent, which can lead to familial
GISTs.

PDGFRA gene mutations associated with GISTs create a protein that no longer
requires binding of the platelet-derived growth factor protein to be activated. As a
result, the PDGFRA protein and the signaling pathways are constitutively activated,
which increases cell proliferation and survival, leading to tumor formation.

Other disorders

PDGFRA gene mutations that lead to a constitutively active PDGFRA protein are also
associated with inflammatory fibroid polyps, which are small, noncancerous (benign)
tumors that form in the gastrointestinal tract. These tumors are made up of fibrous
tissue and usually contain cells known to cause inflammation (inflammatory cells). As
in GISTs, the constitutively active PDGFRA protein leads to the overgrowth of cells
and formation of tumors.

Chromosomal Location

Cytogenetic Location: 4q12, which is the long (q) arm of chromosome 4 at position 12
Molecular Location: base pairs 54,229,089 to 54,298,247 on chromosome 4 (Homo
sapiens Annotation Release 109, GRCh38.p12) (NCBI)

Credit: Genome Decoration Page/NCBI
Other Names for This Gene

- CD140 antigen-like family member A
- CD140A
- CD140a antigen
- GAS9
- PDGFR-alpha
- PDGFR2
- PGFRA_HUMAN
- platelet-derived growth factor receptor 2
- platelet-derived growth factor receptor alpha
- platelet-derived growth factor receptor, alpha polypeptide

Additional Information & Resources

Educational Resources

- Developmental Biology (sixth edition, 2000): The RTK Pathway
  https://www.ncbi.nlm.nih.gov/books/NBK10043/#A1053

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28PDGFRA%5BTI%5D
  %29+OR+%28platelet-derived+growth+factor+receptor+alpha%5BTI%5D
  %29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena
  %5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+
  %22last+720+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- PLATELET-_DERIVED GROWTH FACTOR RECEPTOR, ALPHA
  http://omim.org/entry/173490

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/PDGFRAID143ch4q12.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PDGFRA%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5156
Sources for This Summary

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