PDGFRA Gene

Subjects: Genetics
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Definition

platelet derived growth factor receptor alpha

1. Introduction

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.

2. Health Conditions Related to Genetic Changes

2.1. 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.

2.2. 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.

2.3. 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.

3. 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

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Keywords

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