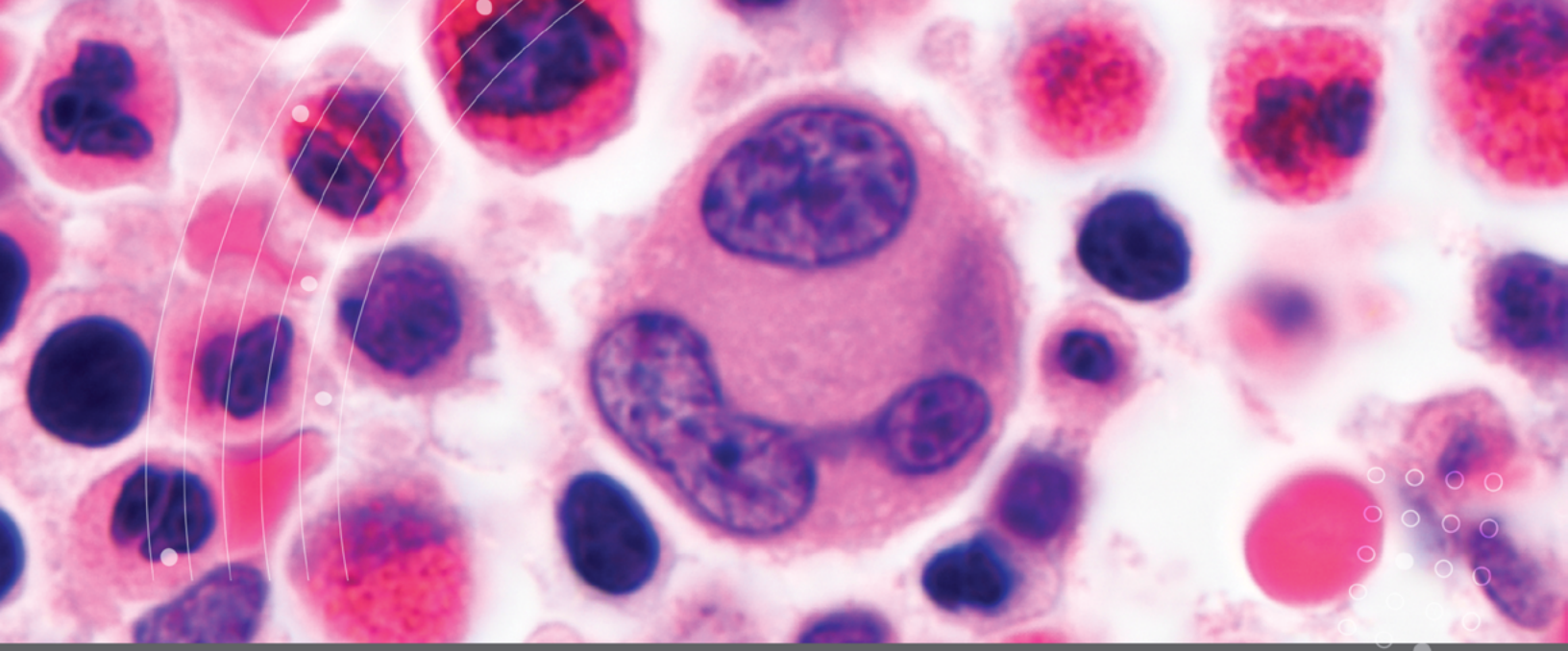


National Human Genome Research Institute

# RUNX1 Familial Platelet Disorder Factsheet

## What is RUNX1 Familial Platelet Disorder with Associated Myeloid Malignancies?

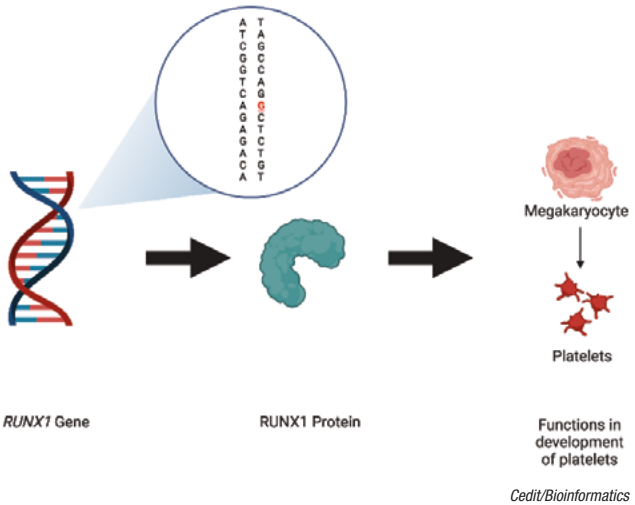
*RUNX1* Familial Platelet Disorder (*RUNX1*-FPD) is a rare condition that can affect many parts of the body and results in higher risk for developing certain cancers. This condition is caused by harmful changes in the *RUNX1* gene. A parent can pass down these genetic changes to their children, which means that multiple people in the same family can have *RUNX1*-FPD. When someone is diagnosed with *RUNX1*-FPD, certain medications and cancer screenings may be recommended. *RUNX1*-FPD is also sometimes called *RUNX1* Familial Platelet Disorder with associated myeloid malignancies (*RUNX1*-FPDMM).

## What is the *RUNX1* gene?

Genes provide instructions for proteins that make our bodies work. Harmful changes in our genes, called pathogenic variants or mutations, can result in proteins that do not work the way they should and can cause a person to develop certain symptoms or conditions.

The *RUNX1* gene provides instructions for a type of protein called a transcription factor. Transcription factors affect the activity of certain genes by binding to them and allowing them to be turned on. The RUNX1 transcription factor affects the activity of genes involved in the development of stem cells in the bone marrow (hematopoietic stem cells), which go on to form blood cells. The *RUNX1* gene also plays a role in embryonic development. The *RUNX1* gene was discovered in 1994 and was initially known by another name (*CBFA2*).

A person with *RUNX1*-FPD is born with a pathogenic variant (a harmful change) in the *RUNX1* gene. This pathogenic variant causes the protein produced by the gene to not work the way it should, leaving the person with only one functioning copy of *RUNX1*. This pathogenic variant affects the stem cells that produce blood cells, which results in the bleeding and bruising symptoms seen in *RUNX1*-FPD as well as the elevated risk for blood-related cancers.

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**For more information**
**genome.gov** | **phone/text** 301.385.5205 | **email** runx1@nih.gov

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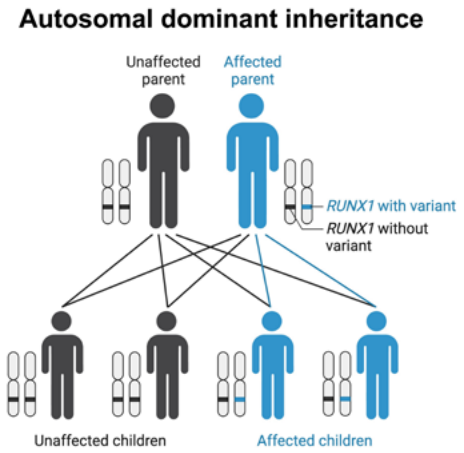
A pathogenic variant can be compared to a spelling error in the gene. There are different types of pathogenic variants (from substitutions, deletions, and insertions in the gene) and different locations within the *RUNX1* gene in which these variants can occur. Researchers are looking into whether and how the specific type or location of the pathogenic variant can put an individual at a higher or lower risk for developing certain symptoms. In the future, details about pathogenic variants could be one of many pieces of information, such as family history, that are used to predict an individual's risk of developing cancer and to determine the appropriate level of screening they should undergo.

## How is the *RUNX1* gene passed through families?

People typically have two copies of the *RUNX1* gene, one copy inherited from each parent. People with *RUNX1*-FPD have a pathogenic variant in one copy of the *RUNX1* gene. Having a pathogenic variant in one of the two copies of the gene is enough to cause *RUNX1*-FPD, meaning that the condition is autosomal dominant. Since each parent passes one copy of each gene to their offspring, there is a 50% chance in each pregnancy that the parent will pass down the copy with the pathogenic variant in *RUNX1*. This means that anyone whose parent has *RUNX1*-FPD has a 50% chance of developing the condition themselves.




## How is the body affected by *RUNX1*-FPD?

There are several signs and symptoms of *RUNX1*-FPD. These may occur in many regions of the body. Not everyone will experience all of these symptoms.

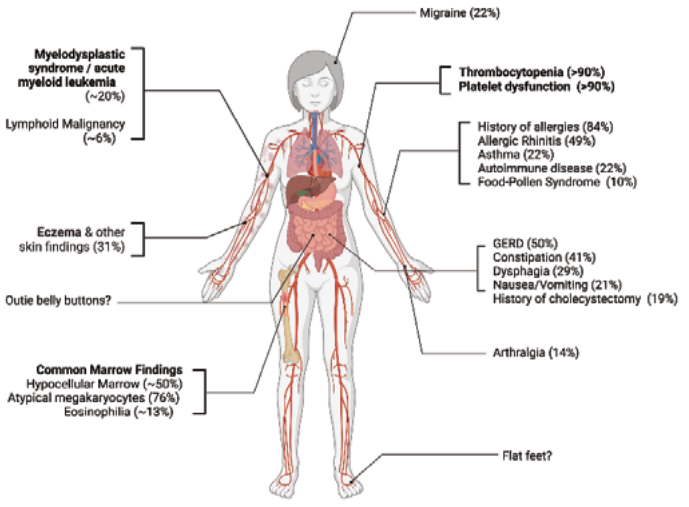
**Platelets.** The most common features associated with *RUNX1*-FPD are having a low number of platelets in the blood (thrombocytopenia) and having platelets that do not work as well as they should (platelet dysfunction). Thrombocytopenia and platelet dysfunction each affect more than 90% of people diagnosed with *RUNX1*-FPD. These changes in a person's blood can result in easy bruising and prolonged bleeding after injury.

**Bone Marrow.** Many individuals with *RUNX1*-FPD also have differences in their bone marrow. These differences can be observed through a bone marrow biopsy. The bone marrow cells that are responsible for creating platelets (megalokaryocytes) are shaped differently (atypical) in 75% of people with *RUNX1*-FPD. About 50% of people also have fewer cells in their bone marrow than expected for their age (hypocellular marrow). An elevated number of white blood cells (eosinophilia) is seen in about 15% of people with *RUNX1*-FPD.

**Skin.** Skin-related symptoms occur in about 30% of people with *RUNX1*-FPD. The most common skin finding observed is eczema (a condition resulting in dry, itchy, inflamed skin). People sometimes have other skin conditions such as psoriasis (a condition that causes a rash with scaly patches).

**Cancer Risk.** Not everyone with *RUNX1*-FPD will develop cancer. However, people with *RUNX1*-FPD have a higher risk to develop some types of cancers. Specifically, they have a 20-50% lifetime risk for developing a blood-related cancer (hematologic malignancy). Risk for cancer appears to cluster in families. In about 45% of families with *RUNX1*-FPD, no one has developed a blood-related cancer. About 55% of families have at least one family member who has developed a blood-related cancer.

The most common types of cancers developed are myelodysplastic syndrome and acute myeloid leukemia. Less commonly, people may develop lymphoma or acute lymphoblastic leukemia, collectively known as lymphoid malignancies, or other types of blood-related cancers. Anaplastic anemia and smoldering myeloma have also been observed in some people with *RUNX1*-FPD.

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**Immune System.** There are several conditions related to the immune system that are more common in people with *RUNX1*-FPD. Allergies are experienced by 85% of people, with 50% of people having experienced hay fever (allergic rhinitis). Asthma occurs in 20% of people. Autoimmune diseases are also reported in 20% of individuals. Joint pain (arthralgia) is reported in 15% of people. Food-Pollen syndrome is reported in 10% of people.
**Gastrointestinal.** Several gastrointestinal symptoms have also been reported. About 50% of people with *RUNX1*-FPD experience gastroesophageal reflux disease (GERD), also known as acid reflux. Constipation occurs in 40% of people. About 30% report difficulty swallowing (dysphagia). Frequent nausea and/or vomiting occur in about 20% of people with *RUNX1*-FPD. Finally, about 20% of individuals report having undergone a removal of the gallbladder (cholecystectomy) for the treatment of gallstones.

**Other features.** There are some potential features of *RUNX1*-FPD that are still under investigation. Some people with *RUNX1*-FPD may be more sensitive to pain. Some may also be less sensitive to warm temperatures. People with *RUNX1*-FPD seem to have flat feet and/or outie belly buttons more frequently. Research into these features is ongoing.

## How is *RUNX1*-FPD managed?

A person diagnosed with *RUNX1*-FPD should see a blood specialist (hematologist) for an evaluation. The hematologist will conduct several blood tests and may suggest a bone marrow biopsy. People with *RUNX1*-FPD should also see a dermatologist. The dermatologist will conduct a clinical evaluation for eczema and other skin concerns as necessary. People with *RUNX1*-FPD should also see a genetic counselor for genetic testing and to discuss the implications of their diagnosis for themselves and their family. The genetic counselor may recommend additional testing for family members.

Monitoring for the development of cancer can look different for everyone depending on testing results, family history of cancer, and other lifestyle factors, so a doctor will make a specific recommendation for each patient. However, the current general recommendation is for people with *RUNX1*-FPD to have a bone marrow biopsy every year and/or a blood test called a complete blood count (CBC) every 3-6 months. If the screening tests show signs that a cancer may be developing, early treatments can be offered. The person may be eligible for a stem cell transplant.

Managing bleeding and bruising symptoms is also personalized by an individual's medical team. If someone is having a surgery or experiences an injury, the medical team may recommend certain treatments to help stabilize blood clots or platelet transfusions if necessary. As of today, researchers are working to establish clinical guidelines and precision treatment of *RUNX1*-FPD.

## Living with *RUNX1*-FPD

Living with a health condition can be challenging. Research into the lived experiences of people with *RUNX1*-FPD is ongoing. However, there is evidence that some of these individuals may experience higher than typical levels of pain, tiredness, anxiety, or depression. If you feel that you are experiencing challenges to your mental health, please reach out to a qualified mental health professional. Individual therapy can be helpful to some people. You could also consider connecting with a support group for people living with a genetic condition or an elevated risk for cancer.

Many people living with a genetic condition like *RUNX1*-FPD find it helpful to connect with others who are also affected with the condition. It is often easiest to connect with others online, such as through social media groups. Disease communities can share resources, provide support, and offer a deep understanding of the experience of living with *RUNX1*-FPD. However, it is important to keep in mind that while others may have similar experiences to you, symptoms and outcomes differ between families and individuals. Not everyone will experience the same symptoms due to *RUNX1*-FPD. Further, it is important to treat health information found online with caution, whether it is from another individual or online research. Confirm any information you are unsure about with a healthcare provider, genetic counselor, or a member of the research team.

You may have questions about talking to children about *RUNX1*-FPD. Please refer to the team's Familial Communication Guide for suggestions. If you have questions about passing on this condition to future generations or if you are considering having children and would like to talk about reproductive options, please make an appointment with a prenatal genetic counselor. Individuals in the United States and Canada can use the following link to locate a genetic counselor: https://findageneticcounselor.nsgc.org.

## Glossary

Refer to the Familial Communication Guide glossary for further definition of terms.