

MPL Gene

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1. Introduction

The *MPL* gene provides instructions for making the thrombopoietin receptor protein, which promotes the growth and division (proliferation) of cells. This receptor is especially important for the proliferation of certain blood cells called megakaryocytes, which produce platelets, the cells involved in blood clotting. Research suggests that the thrombopoietin receptor may also play a role in the maintenance of hematopoietic stem cells, which are stem cells located within the bone marrow that have the potential to develop into red blood cells, white blood cells, and platelets.

The thrombopoietin receptor is turned on (activated) when a protein called thrombopoietin attaches (binds) to it. The activated thrombopoietin receptor stimulates a signaling pathway called the JAK/STAT pathway, which transmits chemical signals from outside the cell to the cell's nucleus and is important for controlling the production of blood cells.

2. Health Conditions Related to Genetic Changes

2.1. Essential thrombocythemia

Several mutations in the *MPL* gene have been associated with a small number of cases of essential thrombocythemia, a condition characterized by an increased number of platelets in the blood. Platelets are the blood cells involved in blood clotting, and abnormal clotting (thrombosis) is common in people with essential thrombocythemia.

MPL gene mutations associated with essential thrombocythemia change a single protein building block (amino acid) in the thrombopoietin receptor protein. An inherited form of the condition, called familial essential thrombocythemia, is caused by an *MPL* gene mutation that results in the replacement of the amino acid serine with the amino acid asparagine at position 505 in the protein (written as Ser505Asn or S505N). Essential thrombocythemia that does not run in families (sporadic essential thrombocythemia) has been associated with *MPL* gene mutations that result in the replacement of the amino acid tryptophan at position 515 with another amino acid, most commonly leucine. These mutations are generally referred to as W515 mutations.

Amino acid changes at position 505 or 515 result in a thrombopoietin receptor protein that is constantly turned on (constitutively activated), which, in essential thrombocythemia, leads to the overproduction of abnormal megakaryocytes and an increased number of platelets. Excess platelets can cause thrombosis, which leads to many signs and symptoms of essential thrombocythemia.

2.2. Primary myelofibrosis

Several mutations in the *MPL* gene have been identified in some people with primary myelofibrosis. This condition is characterized by scar tissue (fibrosis) in the bone marrow, the tissue that produces blood cells.

Like essential thrombocythemia, primary myelofibrosis is associated with the *MPL* gene mutations referred to as W515 mutations. These mutations lead to a constitutively activated thrombopoietin receptor protein, which results in the overproduction of abnormal megakaryocytes. These megakaryocytes stimulate other cells to release collagen, a protein that normally provides structural support for the cells in the bone marrow but causes scar tissue formation in primary myelofibrosis. Because of the fibrosis, the bone marrow cannot produce enough normal blood cells, leading to the signs and symptoms of the condition.

It is unknown how the same gene mutations can be associated with different conditions.

2.3. Other disorders

Mutations in the *MPL* gene cause a rare condition called congenital amegakaryocytic thrombocytopenia (CAMT). This condition begins in infancy and is characterized by low numbers of megakaryocytes (megakaryocytopenia) and platelets (thrombocytopenia). CAMT can lead to an impairment of bone marrow function known as bone marrow failure.

The *MPL* gene mutations involved in CAMT lead to a reduced functioning or nonfunctioning thrombopoietin receptor protein. People with no thrombopoietin receptor function have a severe form of the condition called CAMT I. People with some remaining thrombopoietin receptor function have a milder form of the condition called CAMT II.

3. Other Names for This Gene

- C-MPL
- CD110
- MPLV
- myeloproliferative leukemia protein
- myeloproliferative leukemia virus oncogene
- proto-oncogene c-Mpl
- thrombopoietin receptor
- thrombopoietin receptor precursor
- TPO-R
- TPOR
- TPOR_HUMAN

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