WAS gene

WASP actin nucleation promoting factor

Normal Function

The *WAS* gene provides instructions for making a protein called WASP. This protein is found in all blood cells. WASP is involved in relaying signals from the surface of blood cells to the actin cytoskeleton, which is a network of fibers that make up the cell's structural framework. WASP signaling triggers the cell to move and attach to other cells and tissues (adhesion). In white blood cells, which protect the body from infection, this signaling allows the actin cytoskeleton to establish the interaction between cells and the foreign invaders that they target (immune synapse).

Health Conditions Related to Genetic Changes

Wiskott-Aldrich syndrome

More than 350 mutations in the *WAS* gene have been found to cause Wiskott-Aldrich syndrome, a condition characterized by abnormal immune system function (immune deficiency) and a reduced ability to form blood clots leading to prolonged bleeding episodes.

Most of the mutations lead to the production of an abnormally short, nonfunctional version of WASP or prevent the production of any WASP. As a result, WASP cannot relay signals, which disrupts the function of the actin cytoskeleton in developing blood cells.

White blood cells that lack WASP have a decreased ability to respond to their environment and form immune synapses. As a result, white blood cells are less able to respond to foreign invaders, causing many of the immune problems related to Wiskott-Aldrich syndrome. Similarly, when cells that aid blood clot formation (platelets) lack functional WASP, their development is impaired. A reduction in platelet size and early cell death leads to the bleeding problems in affected individuals. The impairments of white blood cells and platelets are largely responsible for the immune deficiency and bleeding problems characteristic of Wiskott-Aldrich syndrome.

X-linked thrombocytopenia

More than 60 mutations in the *WAS* gene have been found to cause X-linked

thrombocytopenia, a blood disorder characterized by a decrease in the amount and size of platelets, leading to prolonged bleeding episodes. Immune problems such as an increased susceptibility to infections may also occur.

Most of these *WAS* gene mutations change single protein building blocks (amino acids) in WASP. Mutations typically lead to the production of an altered protein that cannot efficiently relay signals from the cell membrane to the actin cytoskeleton. In people with X-linked thrombocytopenia, these signaling problems primarily affect the development of platelets. In some cases, white blood cells are affected. When WASP function is impaired in white blood cells, these cells are less able to respond to foreign invaders and immune disorders are more likely to occur.

Some *WAS* gene mutations cause X-linked thrombocytopenia in some individuals and a related condition called Wiskott-Aldrich syndrome (described above) in others. These mutations usually prevent the production of any WASP. It is unknown why some people with these mutations have the relatively mild features of X-linked thrombocytopenia and others have the severe symptoms of Wiskott-Aldrich syndrome. Because they have overlapping features and the same genetic cause, Wiskott-Aldrich syndrome, X-linked thrombocytopenia, and severe congenital neutropenia are sometimes collectively referred to as WAS-related disorders.

Severe congenital neutropenia

MedlinePlus Genetics provides information about Severe congenital neutropenia

Other Names for This Gene

- IMD2
- WASP
- WASP_HUMAN
- WASPA

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of WAS (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7454[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28WAS%5BTIAB%5D%29+OR+%28WASP%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+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- WASP ACTIN NUCLEATION PROMOTING FACTOR; WAS (https://omim.org/entry/300392)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7454)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=WAS[gene])

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Genomic Location

The *WAS* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

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