

STAT1 Gene

Subjects: **Genetics & Heredity**

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Signal transducer and activator of transcription 1: The STAT1 gene provides instructions for making a protein that is involved in multiple immune system functions, including the body's defense against a fungus called *Candida*.

genes

1. Normal Function

The *STAT1* gene provides instructions for making a protein that is involved in multiple immune system functions, including the body's defense against a fungus called *Candida*. When the immune system recognizes *Candida*, it generates cells called Th17 cells. These cells produce signaling molecules (cytokines) called the interleukin-17 (IL-17) family as part of an immune process called the IL-17 pathway. The IL-17 pathway creates inflammation, sending other cytokines and white blood cells that fight foreign invaders and promote tissue repair. In addition, the IL-17 pathway promotes the production of certain antimicrobial protein segments (peptides) that control growth of *Candida* on the surface of mucous membranes.

The STAT1 protein helps keep the immune system in balance by controlling the IL-17 pathway. When the STAT1 protein is turned on (activated), it blocks (inhibits) this pathway.

In contrast to its inhibitory role in the IL-17 pathway, the STAT1 protein helps promote other immune processes called the interferon-alpha/beta (IFNA/B) and interferon-gamma (IFNG) signaling pathways. The IFNA/B pathway is important in defense against viruses, and the IFNG pathway helps fight a type of bacteria called mycobacteria, which includes the bacterium that causes tuberculosis.

2. Health Conditions Related to Genetic Changes

2.1. Familial candidiasis

At least 35 *STAT1* gene mutations have been identified in people with familial candidiasis, an inherited tendency to develop infections caused by the *Candida* fungus (commonly called yeast infections). Most people with familial candidiasis have chronic infections of the skin, nails, and mucous membranes such as the lining of the mouth, collectively called chronic mucocutaneous candidiasis, beginning in early childhood. Some people with *STAT1* gene mutations have additional features such as increased susceptibility to other infections and an increased risk

of autoimmune disorders, in which the immune system attacks the body's own tissues or organs. This combination of signs and symptoms caused by *STAT1* gene mutations is sometimes called immunodeficiency 31C.

The *STAT1* gene mutations that have been identified in people with familial candidiasis are described as "gain of function" because they increase the amount of activated STAT1 protein in cells. By increasing STAT1's inhibitory effect on the IL-17 pathway, the mutations impair the body's ability to fight *Candida* and result in the chronic infection that occurs in familial candidiasis. The effects of the increase in activated STAT1 protein on other signaling pathways are thought to underlie the variety of features that can occur in immunodeficiency 31C, but the specific mechanisms are not well understood.

2.2. Other disorders

STAT1 gene mutations can also cause other immune system problems called immunodeficiency 31A and immunodeficiency 31B. In contrast with the gain-of-function mutations associated with familial candidiasis (described above), these *STAT1* gene mutations are described as "loss-of-function" mutations because they impair or eliminate the protein's normal action. The *STAT1* gene mutations that cause immunodeficiency 31A impair the STAT1 protein's function in the IFNG pathway, resulting in an increased susceptibility to mycobacteria. In the more severe disorder immunodeficiency 31B, the *STAT1* gene mutations impair both the IFNG pathway and the IFNA/B pathway, resulting in susceptibility to both viral infections such as herpes simplex and viral encephalitis, and mycobacterial infections such as tuberculosis.

3. Other Names for This Gene

- IMD31A
- IMD31B
- IMD31C
- ISGF-3
- signal transducer and activator of transcription 1, 91kDa
- signal transducer and activator of transcription-1
- STAT91
- transcription factor ISGF-3 components p91/p84

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