HLA-B Gene

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1. Introduction

The *HLA-B* gene provides instructions for making a protein that plays a critical role in the immune system. *HLA-B* is part of a family of genes called the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria.

HLA is the human version of the major histocompatibility complex (MHC), a gene family that occurs in many species. Genes in this complex are categorized into three basic groups: class I, class II, and class III. In humans, the *HLA-B* gene and two related genes, *HLA-A* and *HLA-C*, are the main genes in MHC class I.

MHC class I genes provide instructions for making proteins that are present on the surface of almost all cells. On the cell surface, these proteins are bound to protein fragments (peptides) that have been exported from within the cell. MHC class I proteins display these peptides to the immune system. If the immune system recognizes the peptides as foreign (such as viral or bacterial peptides), it responds by triggering the infected cell to self-destruct.

The *HLA-B* gene has many possible variations, allowing each person's immune system to react to a wide range of foreign invaders. Hundreds of versions (alleles) of the *HLA-B* gene are known, each of which is given a particular number (such as *HLA-B27*). Closely related alleles are categorized together; for example, more than 60 very similar alleles are subtypes of *HLA-B27*. These subtypes are designated as *HLA-B*2701* to *HLA-B*2763*.

2. Health Conditions Related to Genetic Changes

2.1. Ankylosing Spondylitis

Several variations of the *HLA-B* gene increase the risk of developing ankylosing spondylitis, particularly a version called *HLA-B27*. It is uncertain how this variation causes the increased risk. Researchers speculate that *HLA-B27* may abnormally display peptides that trigger an immune reaction, resulting in the inflammatory process that causes arthritis. Other research suggests that the joint inflammation characteristic of this disorder may result from improper folding of the *HLA-B27* protein or the presence of abnormal forms of the protein on the cell surface. Although many people with ankylosing spondylitis have the *HLA-B27* variation, most people with this version of the *HLA-B* gene never develop the disorder. Additional genetic and environmental factors, many of which are unknown, affect the chances of developing ankylosing spondylitis and influence its progression

2.2. Behçet Disease

Several versions of the *HLA-B* gene, particularly *HLA-B51*, are associated with an increased risk of developing Behçet disease, a chronic inflammatory condition that affects many parts of the body. This association is strongest in people from Japan, the Middle East, and other parts of Asia. Researchers do not know how *HLA-B51* increases the risk of this disorder. Although many people with Behçet disease have the *HLA-B51* variation, most people with this version of the *HLA-B* gene never develop the condition. It appears likely that other factors, such as viral or bacterial infections and changes in other genes, also influence the development of this complex disorder.

2.3. Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis

Several variations of the *HLA-B* gene have been studied as risk factors for Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), a potentially life-threatening skin reaction most often triggered by medications. For example, the variation *HLA-B*1502* increases the risk of SJS/TEN in people taking certain medications used to treat seizures, particularly a drug called carbamazepine. This version of the gene is most common among people of Han Chinese or southeast Asian descent. Another version of the gene, *HLA-B*5801*, increases the risk of SJS/TEN in people treated with allopurinol (a drug used to treat kidney stones and gout, which is a form of arthritis caused by a buildup of uric acid in the joints). This association has been confirmed in southeast Asians and in people of non-Asian ancestry, although *HLA-B*5801* occurs less frequently in non-Asian populations.

Studies suggest that the *HLA-B* gene variations associated with SJS/TEN cause the immune system to react abnormally to some medications. In a process that is not well understood, the triggering drug causes immune cells called cytotoxic T cells and natural killer (NK) cells to release a substance called granulysin. This substance destroys cells in the skin and mucous membranes, including the lining of the mouth and the airways. The death of these cells causes severe blistering and peeling that can have life-threatening effects.

Most people who have variations in the *HLA-B* gene that are associated with an increased risk of SJS/TEN never develop the condition, even if they are exposed to drugs that can trigger it. Researchers believe that additional genetic and nongenetic factors, many of which are unknown, likely play a role in whether a particular individual develops SJS/TEN.

2.4. Other Disorders

The *HLA-B27* variant is associated with a group of inflammatory joint diseases related to ankylosing spondylitis. These conditions are known as spondyloarthropathies. Some of these disorders are associated with a common skin condition called psoriasis or with chronic disorders that cause inflammation of the intestinal walls (inflammatory bowel disease). One of the spondyloarthropathies, reactive arthritis, is typically triggered by bacterial infections of the gastrointestinal or genital tract. Following an infection, affected individuals may develop arthritis, back pain, and eye inflammation. Like ankylosing spondylitis, many factors probably contribute to the development of reactive arthritis and other spondyloarthropathies.

Among people with human immunodeficiency virus (HIV) infection, a version of the *HLA-B* gene designated *HLA-B*5701* increases the risk of an adverse reaction (hypersensitivity) to the drug abacavir. This medication slows the spread of the HIV-1 virus in the body. People with abacavir hypersensitivity often develop a fever, chills, rash, upset stomach, and other symptoms when treated with this drug.

Several variations of the *HLA-B* gene appear to play a role in the progression of HIV infection to acquired immunodeficiency syndrome (AIDS). AIDS is a disease that damages the immune system, preventing it from effectively defending the body against infections. The signs and symptoms of AIDS may not appear until 10 or more years after infection with HIV. Studies suggest that people with HIV infection who have *HLA-B27* or *HLA-B57* tend to progress more slowly than usual to AIDS. On the other hand, researchers believe that HIV-positive individuals who have *HLA-B35* tend to develop the signs and symptoms of AIDS more quickly than usual. Other factors also influence the progression of HIV infection to AIDS.

Another version of the *HLA-B* gene, *HLA-B53*, has been shown to help protect against severe malaria, a disease caused by a parasite that is carried by mosquitoes. *HLA-B53* is most common in West African populations, where malaria is a frequent cause of death in children. Studies suggest that this version of the *HLA-B* gene may help the immune system respond more effectively to the parasite that causes malaria.

3. Other Names for This Gene

- 1B07_HUMAN
- HLA class I histocompatibility antigen, B alpha chain
- leukocyte antigen B
- MHC class I HLA-B heavy chain

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