

Human HLA-B

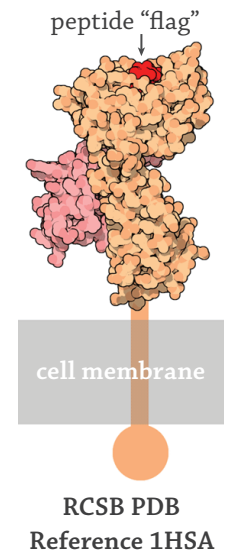
Protein Function

T-cells in the immune system find and destroy threats to the body like harmful bacteria, viruses, and toxins. To do that, T-cells need a way to tell the difference between stuff that is “self” and stuff that is “not self.”

For instance, when a virus enters a cell it begins producing proteins to control the host cell and replicate itself. When these proteins are identified as abnormal, they’re sent through a protein shredding machine that breaks the protein into tiny pieces, called peptides.

These “non-self” peptides are passed to Human Leukocyte Antigen (HLA-B) proteins tethered to the outside of the cell. HLA-B proteins have grooves that hold these peptide fragments. The peptides stick out of the groove and act as “self” or “not self” flags.

During early childhood, HLA-B proteins help teach newborn T-cells the difference between “self” and “not self” peptide flags. Then, throughout the rest of our lives, they present “not self” peptide flags to T-cells. This signals the T-cell to destroy the foreign invader.



High Protein Variability

We are constantly being exposed to pathogens and toxins. To respond to new threats, it is advantageous to the population if our HLA-B proteins can bind to and present a wide variety of peptide flags.



HLA-B, partial amino acid
sequence (11 of 362 total)

For this reason, HLA-B is the most highly variable gene in the human genome. Even a single base change can alter how or if the protein binds to a particular peptide. Without mutation, HLA-B simply couldn’t keep doing its job.

Scientists have identified several thousand HLA-B alleles. Depending on where your ancestors lived and what diseases they were able to survive, you have a unique set of HLA-B proteins selected to help identify previously encountered invaders.

HLA-B Alleles & Health

Which mutations you carry in your HLA-B genes can impact health – in both positive and negative ways:

- In organ transplants, if the donor and recipient HLA-B alleles don’t match, the organ has a high likelihood of being rejected as “not self.” That’s why organ transplants work best with close relatives.
- Several HLA-B alleles are linked to bad drug reactions. In people with these alleles, taking certain drugs causes T-cells to release a substance that destroys mucus membranes such as the airways, making it difficult to breathe.
- Inflammation is an immune response that causes swelling around foreign material. Several HLA-B alleles cause this response to go wrong, resulting in conditions like ankylosing spondylitis, a severe joint disorder.
- Some HLA-B alleles can improve the body’s response to specific infections. The B35 allele can protect you from malaria, while the B27 allele can help you fight off HIV.

HLA-B: Mutated Segment Existing Variations

The gene segment you just mutated is a sequence from a real gene called HLA-B. It turns out that HLA-B is an extremely variable gene. In fact, chances are pretty high that, if you chose to do a substitution, your mutation exists in an actual person.

The reference sequence below is a composite of 8 different versions of the gene assembled by four different teams of scientists. Reference sequences are used to catalog and study gene variations. Reference sequences don't necessarily represent the most common variations for the sequence.

Compare your mutated protein sequence to the reference sequence and known variations below.

reference amino acid sequence	M	Y	W	D	R	N	T	Q	I	Y	K
REFERENCE DNA SEQUENCE	A T G	T G G	G A C	C G G	A A C	A A C	A C A	C A G	A T C	T A C	A A G
Ankylosing Spondylitis (B27)	T A T	T G G	G A C	C G G	G A C	G A C	A C A	C A G	A T C	T G C	A A G
Increased Malaria Protection (B35)	T A T	T G G	G A C	C G G	A A C	A A C	A C A	C A G	A T C	T G C	A A G
Better-Than-Average HIV Prognosis (B57)	T A T	T G G	G A C	C G G	G A C	G A C	A C A	C G G	A A C	A T G	A A G
Bad reaction to a certain seizure medicine (B15)	T A T	T G G	G A C	C G G	G A C	G A C	A C A	C A G	A T C	T C C	A A G
Bad reaction to certain kidney stone medicine (B58)	T A T	T G G	G A C	G G G	G A C	G A C	A C A	C G G	A A C	A T G	A A G

Alleles Associated with Medical Outcomes	M	Y	W	D	R	N	T	Q	I	Y	K
Example Variations Found in Other Alleles	C T C	C A A	A T A	A T A	G T A	G T A	G T C	A G A	C A A	A A C	A A G
	G C C	C C C	G G T	G G T	G G T	G G T	G G T	C G G	C G G	C G T	G T

different amino acid

changed to stop codon

deletion

insertion