MYD88 gene

MYD88 innate immune signal transduction adaptor

Normal Function

The *MYD88* gene provides instructions for making a protein involved in signaling within immune cells. The MyD88 protein acts as an adapter, connecting proteins that receive signals from outside the cell to the proteins that relay signals inside the cell. In particular, MyD88 transfers signals from certain proteins called Toll-like receptors and interleukin-1 (IL-1) receptors, which are important for an early immune response to foreign invaders such as bacteria. In response to signals from these receptors, the MyD88 adapter protein stimulates signaling molecules that turn on a group of interacting proteins known as nuclear factor-kappa-B. Nuclear factor-kappa-B regulates the activity of multiple genes, including genes that control the body's immune responses and inflammatory reactions. It also protects cells from certain signals that would otherwise cause them to self-destruct (undergo apoptosis).

Health Conditions Related to Genetic Changes

MyD88 deficiency

At least four mutations in the *MYD88* gene have been found to cause a condition called MyD88 deficiency. Individuals with this condition develop recurrent bacterial infections. Unlike in Waldenström macroglobulinemia and other blood disorders (described below), the gene mutations that cause *MYD88* deficiency are inherited and are found in every cell of the body (known as germline mutations). These mutations result in the production of a nonfunctional protein or no protein at all. As a result, the protein cannot relay signals that stimulate an immune response, which allows multiple severe infections to develop.

Waldenström macroglobulinemia

A particular mutation in the *MYD88* gene is found in more than 90 percent of people with Waldenström macroglobulinemia. This rare form of blood cancer is characterized by an excess of abnormal white blood cells called lymphoplasmacytic cells in the bone marrow and overproduction of a protein called IgM. The mutation involved in this condition changes a single protein building block (amino acid) in the MyD88 protein, replacing the amino acid leucine with the amino acid proline at position 265 (written as Leu265Pro or L265P). The mutation is acquired during a person's lifetime and is present

only in the abnormal white blood cells. This type of genetic change, called a somatic mutation, is not inherited. Waldenström macroglobulinemia is thought to result from multiple genetic changes, including the *MYD88* gene mutation.

The altered MyD88 protein is constantly functioning (overactive). It stimulates the signaling molecules that activate nuclear factor-kappa-B, even without signals from outside the cell. Researchers suggest that abnormally active nuclear factor-kappa-B allows survival of abnormal cells that should undergo apoptosis, which may contribute to the accumulation of lymphoplasmacytic cells in Waldenström macroglobulinemia.

Other disorders

The L265P mutation is also found in about 50 to 80 percent of cases of a blood disorder called IgM monoclonal gammopathy of undetermined significance (IgM-MGUS). Individuals with this condition have slightly elevated levels of IgM in the blood. IgM-MGUS can transform into Waldenström macroglobulinemia (described above) or other blood cell cancers or disorders; when the *MYD88* gene mutation is present in IgM-MGUS, the condition is more likely to progress.

Other cancers

The somatic L265P mutation in the *MYD88* gene is also found in some cases of other blood cell cancers, including diffuse large B-cell lymphoma (DLBCL) and marginal zone lymphoma. The mechanism by which the mutation contributes to development of the condition is thought to be the same as in Waldenström macroglobulinemia (described above). The type of cancer that develops is likely determined by the type of cell that acquires the L265P mutation. This mutation is thought to be one of many genetic changes involved in the development of these cancers.

Other Names for This Gene

- MYD88_HUMAN
- MYD88D
- myeloid differentiation primary response 88
- myeloid differentiation primary response gene (88)
- myeloid differentiation primary response protein MyD88

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MYD88 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4615[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28MYD88%5BTI%5D%29+OR+%28myeloid+differentiation+primary+response+88%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+360+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- MYD88 INNATE IMMUNE SIGNAL TRANSDUCTION ADAPTOR; MYD88 (https://omim.org/entry/602170)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4615)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=MYD88[gene])

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Genomic Location

The *MYD88* gene is found on chromosome 3 (https://medlineplus.gov/genetics/chromosome/3/).

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