MyD88 deficiency

Description

MyD88 deficiency is an inherited disorder of the immune system (primary immunodeficiency). This primary immunodeficiency affects the innate immune response, which is the body's early, nonspecific response to foreign invaders (pathogens). MyD88 deficiency leads to abnormally frequent and severe infections by a subset of bacteria known as pyogenic bacteria. (Infection with pyogenic bacteria causes the production of pus.) However, affected individuals have normal resistance to other common bacteria, viruses, fungi, and parasites. The most common infections in MyD88 deficiency are caused by the *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* bacteria. Most people with this condition have their first bacterial infection before age 2, and the infections can be life-threatening in infancy and childhood. Infections become less frequent by about age 10.

Children with MyD88 deficiency develop invasive bacterial infections, which can involve the blood (septicemia), the membrane covering the brain and spinal cord (meningitis), or the joints (leading to inflammation and arthritis). Invasive infections can also cause areas of tissue breakdown and pus production (abscesses) on internal organs. In addition, affected individuals can have localized infections of the ears, nose, or throat. Although fever is a common reaction to bacterial infections, many people with MyD88 deficiency do not at first develop a high fever in response to these infections, even if the infection is severe.

Frequency

The prevalence of MyD88 deficiency is unknown. At least 24 affected individuals have been described in the medical literature.

Causes

MyD88 deficiency is caused by mutations in the *MYD88* gene, which provides instructions for making a protein that plays an important role in stimulating the immune system to respond to bacterial infection. The MyD88 protein is part of a signaling pathway that is involved in early recognition of pathogens and the initiation of inflammation to fight infection. This signaling pathway is part of the innate immune response.

Mutations in the *MYD88* gene lead to the production of a nonfunctional protein or no protein at all. The loss of functional MyD88 protein prevents the immune system from triggering inflammation in response to pathogens that would normally help fight the infections. Because the early immune response is insufficient, bacterial infections occur often and become severe and invasive.

Researchers suggest that as the immune system matures, other systems compensate for the loss of MyD88 protein, accounting for the improvement in the condition that occurs by adolescence.

Learn more about the gene associated with MyD88 deficiency

- MYD88

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- MYD88 deficiency
- Pyogenic bacterial infections due to MyD88 deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Pyogenic bacterial infections due to MyD88 deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2677092/)

Genetic and Rare Diseases Information Center

- Bacterial susceptibility due to TLR signaling pathway deficiency (https://rarediseases.info.nih.gov/diseases/12638/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- IMMUNODEFICIENCY 68; IMD68 (https://omim.org/entry/612260)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28MyD88+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

References

- Maglione PJ, Simchoni N, Black S, Radigan L, Overbey JR, Bagiella E, BusselJB, Bossuyt X, Casanova JL, Meyts I, Cerutti A, Picard C, Cunningham-Rundles C.IRAK-4 and MyD88 deficiencies impair IgM responses against T-independentbacterial antigens. Blood. 2014 Dec 4;124(24):3561-71. doi:10.1182/blood-2014-07-587824. Epub 2014 Oct 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25320238) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4256908/)
- Picard C, Casanova JL, Puel A. Infectious diseases in patients with IRAK-4,MyD88, NEMO, or IkappaBalpha deficiency. Clin Microbiol Rev. 2011 Jul;24(3):490-7. doi:10.1128/CMR.00001-11. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21734245) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3131061/)
- Picard C, von Bernuth H, Ghandil P, Chrabieh M, Levy O, Arkwright PD, McDonaldD, Geha RS, Takada H, Krause JC, Creech CB, Ku CL, Ehl S, Marodi L, Al-Muhsen S,Al-Hajjar S, Al-Ghonaium A, Day-Good NK, Holland SM, Gallin JI, Chapel H, SpeertDP, Rodriguez-Gallego C, Colino E, Garty BZ, Roifman C, Hara T, Yoshikawa H,Nonoyama S, Domachowske J, Issekutz AC, Tang M, Smart J, Zitnik SE, Hoarau C,Kumararatne DS, Thrasher AJ, Davies EG, Bethune C, Sirvent N, de Ricaud D,Camcioglu Y, Vasconcelos J, Guedes M, Vitor AB, Rodrigo C, Almazan F, Mendez M,Arostegui JI, Alsina L, Fortuny C, Reichenbach J, Verbsky JW, Bossuyt X, Doffinger R, Abel L, Puel A, Casanova JL. Clinical features and outcome ofpatients with IRAK-4 and MyD88 deficiency. Medicine (Baltimore). 2010Nov;89(6):403-425. doi: 10.1097/MD.0b013e3181fd8ec3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21057262) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103888/)
- von Bernuth H, Picard C, Jin Z, Pankla R, Xiao H, Ku CL, Chrabieh M, MustaphaIB, Ghandil P, Camcioglu Y, Vasconcelos J, Sirvent N, Guedes M, Vitor AB,Herrero-Mata MJ, Arostegui JI, Rodrigo C, Alsina L, Ruiz-Ortiz E, Juan M, FortunyC, Yague J, Anton J, Pascal M, Chang HH, Janniere L, Rose Y, Garty BZ, Chapel H,Issekutz A, Marodi L, Rodriguez-Gallego C, Banchereau J, Abel L, Li X, ChaussabelD, Puel A, Casanova JL. Pyogenic bacterial infections in humans with MyD88deficiency. Science. 2008 Aug 1;321(5889):691-6. doi: 10.1126/science.1158298. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18669862) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2688396/)
- von Bernuth H, Picard C, Puel A, Casanova JL. Experimental and naturalinfections

in MyD88- and IRAK-4-deficient mice and humans. Eur J Immunol. 2012Dec;42(12): 3126-35. doi: 10.1002/eji.201242683. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23255009) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3752658/)

- Yamamoto T, Tsutsumi N, Tochio H, Ohnishi H, Kubota K, Kato Z, Shirakawa M, Kondo N. Functional assessment of the mutational effects of human IRAK4 and MyD88genes. Mol Immunol. 2014 Mar;58(1):66-76. doi: 10.1016/j.molimm.2013.11.008. Epub2013 Dec 5. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24316379)

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