IRAK-4 deficiency

Description

IRAK-4 deficiency is an inherited disorder of the immune system (primary immunodeficiency). This immunodeficiency leads to recurrent infections by a subset of bacteria known as pyogenic bacteria but not by other infectious agents. (Infection with pyogenic bacteria causes the production of pus.) The most common infections in IRAK-4 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 with age.

Most people with IRAK-4 deficiency have 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 upper respiratory tract, skin, or eyes. Although fever is a common reaction to bacterial infections, many people with IRAK-4 deficiency do not at first develop a high fever in response to these infections, even if the infection is severe.

Frequency

IRAK-4 deficiency is a very rare condition, although the exact prevalence is unknown. At least 49 individuals with this condition have been described in the scientific literature.

Causes

IRAK-4 deficiency is caused by mutations in the *IRAK4* gene, which provides instructions for making a protein that plays an important role in stimulating the immune system to respond to infection. The IRAK-4 protein is part of a signaling pathway that is involved in early recognition of foreign invaders (pathogens) and the initiation of inflammation to fight infection. This signaling pathway is part of the innate immune response, which is the body's early, nonspecific response to pathogens.

Mutations in the *IRAK4* gene lead to the production of a nonfunctional protein or no protein at all. The loss of functional IRAK-4 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.

Learn more about the gene associated with IRAK-4 deficiency

- IRAK4

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

- Interleukin-1 receptor-associated kinase 4 deficiency
- IRAK4 deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Immunodeficiency 67 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1843256/)

Genetic and Rare Diseases Information Center

- Immunodeficiency due to interleukin-1 receptor-associated kinase-4 deficiency (https://rarediseases.info.nih.gov/diseases/10311/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- IMMUNODEFICIENCY 67; IMD67 (https://omim.org/entry/607676)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28irak4+deficiency%5BTIAB%5D%29+OR+%28IRAK-4+deficiency%5BTIAB%5D%29%29+AND+english%5Bl

a%5D+AND+human%5Bmh%5D)

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