DOCK8 immunodeficiency syndrome

Description

DOCK8 immunodeficiency syndrome is a disorder of the immune system. The condition is characterized by recurrent infections that are severe and can be life-threatening. The infections can be caused by bacteria, viruses, or fungi. Skin infections cause rashes, blisters, accumulations of pus (abscesses), open sores, and scaling. People with DOCK8 immunodeficiency syndrome also tend to have frequent bouts of pneumonia and other respiratory tract infections. Other immune system-related problems in people with DOCK8 immunodeficiency syndrome include an inflammatory skin disorder called eczema, food or environmental allergies, and asthma.

DOCK8 immunodeficiency syndrome is characterized by abnormally high levels of an immune system protein called immunoglobulin E (IgE) in the blood; the levels can be more than 10 times higher than normal for no known reason. IgE normally triggers an immune response against foreign invaders in the body, particularly parasitic worms, and plays a role in allergies. It is unclear why people with DOCK8 immunodeficiency syndrome have such high levels of this protein. People with DOCK8 immunodeficiency syndrome also have highly elevated numbers of certain white blood cells called eosinophils (hypereosinophilia). Eosinophils aid in the immune response and are involved in allergic reactions.

Some people with DOCK8 immunodeficiency syndrome have neurological problems, such as paralysis that affects the face or one side of the body (hemiplegia). Blockage of blood flow in the brain or abnormal bleeding in the brain, both of which can lead to stroke, can also occur in DOCK8 immunodeficiency syndrome.

People with DOCK8 immunodeficiency syndrome have a greater-than-average risk of developing cancer, particularly cancers of the blood or skin.

DOCK8 immunodeficiency syndrome is also commonly called autosomal recessive hyper-IgE syndrome. However, researchers have identified several conditions that feature elevated levels of IgE and that follow an autosomal recessive pattern of inheritance. Each of these conditions has its own set of additional signs and symptoms and a different genetic cause. Some doctors consider these conditions forms of hyper-IgE syndrome, while others consider them independent disorders.

Frequency

DOCK8 immunodeficiency syndrome is a rare disorder whose prevalence is unknown.

Causes

DOCK8 immunodeficiency syndrome is caused by mutations in the *DOCK8* gene. The protein produced from this gene plays a critical role in the survival and function of several types of immune system cells. One of the functions of the DOCK8 protein is to help maintain the structure and integrity of immune cells called T cells and NK cells, which recognize and attack foreign invaders, particularly as these cells travel to sites of infection within the body. In addition, the DOCK8 protein is involved in chemical signaling pathways that stimulate other immune cells called B cells to mature and produce antibodies, which are specialized proteins that attach to foreign particles and germs, marking them for destruction.

DOCK8 gene mutations result in the production of little or no functional DOCK8 protein. Shortage of this protein impairs normal immune cell development and function. It is thought that T cells and NK cells lacking DOCK8 protein are abnormal and die too easily, particularly when moving through the layers of skin. A shortage of these immune cells impairs the immune response to foreign invaders, accounting for the severe skin infections common in DOCK8 immunodeficiency syndrome. A lack of DOCK8 protein also impairs B cell maturation and the production of antibodies. Impairment of this type of immune response leads to recurrent respiratory tract infections in people with this disorder. It is unclear how *DOCK8* gene mutations are involved in other features of DOCK8 immunodeficiency syndrome, such as the elevation of IgE levels, and neurological problems.

Learn more about the gene associated with DOCK8 immunodeficiency syndrome

- DOCK8

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

- AR-HIES
- Autosomal recessive HIES
- Autosomal recessive hyper-IgE syndrome
- CID due to DOCK8 deficiency
- Combined immunodeficiency due to DOCK8 deficiency

- DOCK8 deficiency
- Hyper IgE recurrent infection syndrome, autosomal recessive
- Hyper immunoglobulin E syndrome, autosomal recessive
- Hyperimmunoglobulin E recurrent infection syndrome, autosomal recessive
- Hyperimmunoglobulin E syndrome type 2
- Non-skeletal hyper-IgE syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Combined immunodeficiency due to DOCK8 deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4722305/)

Genetic and Rare Diseases Information Center

- Combined immunodeficiency due to DOCK8 deficiency (https://rarediseases.info.nih.gov/diseases/2816/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- HYPER-IgE SYNDROME 2, AUTOSOMAL RECESSIVE, WITH RECURRENT INFECTIONS; HIES2 (https://omim.org/entry/243700)

Scientific Articles on PubMed

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

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