MDA5 deficiency

Description

MDA5 deficiency is a disorder of the immune system (immunodeficiency) that leads to recurrent, severe infections of the lungs and airways (respiratory tract) beginning in infancy. These infections are most frequently caused by rhinovirus (the virus that causes the common cold). Respiratory syncytial virus (RSV) and the influenza (flu) virus may also cause recurrent infections in affected individuals. While infection by these viruses is common in all children, it usually causes mild symptoms and lasts only a short time before being cleared by a healthy immune system. In contrast, individuals with MDA5 deficiency frequently require hospitalization due to the severity of the symptoms caused by the infection. Repeated infections can contribute to chronic lung disease.

Infections usually become less frequent with age in people with MDA5 deficiency, as the body's immune system matures and develops other mechanisms for fighting viruses.

Frequency

MDA5 deficiency is likely a rare disorder. Its prevalence is unknown.

Causes

MDA5 deficiency is caused by mutations in the *IFIH1* gene, which provides instructions for making the MDA5 protein. These mutations lead to production of an altered MDA5 protein that cannot function, resulting in a shortage (deficiency) of MDA5 activity.

The MDA5 protein plays an important role in innate immunity, the body's early, nonspecific response to foreign invaders (pathogens) such as viruses and bacteria. In particular, the protein recognizes a molecule called double-stranded RNA (a chemical cousin of DNA), which certain viruses, including rhinovirus, RSV, and the flu virus, have as their genetic material or produce when they infect cells and copy (replicate) themselves. (Another subset of viruses has DNA as their genetic material.) When the MDA5 protein recognizes pieces of viral RNA inside the cell, it helps turn on the production of immune system proteins called interferons. Interferons stimulate the immune system to fight infections.

Deficiency of MDA5 protein activity reduces interferon production in response to RNA-containing viruses. A lack of the important early immune response stimulated by interferons leads to severe viral infections in infants with MDA5 deficiency.

Learn more about the gene associated with MDA5 deficiency

- IFIH1

Inheritance

The inheritance pattern of MDA5 deficiency is unclear. In some cases, the condition seems to follow 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. In other cases, it appears that the condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- IFIH1 deficiency

Additional Information & Resources

Patient Support and Advocacy Resources

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

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28MDA5+deficiency%5BTIAB%5D%29+OR+%28IFIH1+deficiency%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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