

CARD9 Gene

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caspase recruitment domain family member 9

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1. Normal Function

The *CARD9* gene provides instructions for making an immune system protein that is involved in the body's defense against fungal infections and is particularly important for fighting infection by a fungus called *Candida*. When the immune system recognizes *Candida*, it generates cells called Th17 cells. These cells produce signaling molecules (cytokines) called the interleukin-17 (IL-17) family as part of an immune process called the IL-17 pathway. The IL-17 pathway creates inflammation, sending other cytokines and white blood cells that fight foreign invaders and promote tissue repair. In addition, the IL-17 pathway promotes the production of certain antimicrobial protein segments (peptides) that control growth of *Candida* on the surface of mucous membranes.

In its role in defending against *Candida* on the mucous membranes and skin, the CARD9 protein passes along signals from other types of immune system proteins. Each of these proteins recognizes a different component of the *Candida* cell wall to trigger the production of Th17 cells and launch the immune response.

In addition to its role in protecting mucous membranes from fungal infection, the CARD9 protein is also important in recruiting neutrophils (immune cells that have strong anti-fungal activity) from the blood to protect the brain and other organs from fungal infection.

2. Health Conditions Related to Genetic Changes

2.1. Familial candidiasis

At least 15 *CARD9* gene mutations have been identified in people with familial candidiasis, an inherited tendency to develop infections caused by the *Candida* fungus (commonly called yeast infections). Most people with familial candidiasis have chronic yeast infections of the skin, nails, and mucous membranes. This pattern of signs and symptoms, which is called chronic mucocutaneous candidiasis, typically begins in early childhood. People with familial candidiasis caused by *CARD9* gene mutations can also develop systemic candidiasis, a potentially life-threatening condition in which *Candida* invades the blood and vital organs, especially the brain. Infections caused by additional types of fungi have also been identified in some people with this form of the disorder, which is sometimes called CARD9 deficiency.

Mutations in the *CARD9* gene impair multiple signaling pathways that normally help recognize *Candida* and are thought to block (inhibit) the activity of the IL-17 pathway. Impairment of this pathway diminishes the body's immune response to *Candida*, leading to the chronic or recurrent yeast infections that occur in people with familial candidiasis. The mutations are also thought to impair the recruitment of neutrophils to fight *Candida* infection in the brain and other organs, which can lead to systemic candidiasis.

3. Other Names for This Gene

- caspase recruitment domain family, member 9
 - hCARD9
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