

CARD9 gene

caspace recruitment domain family member 9

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.

Health Conditions Related to Genetic Changes

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.

Other Names for This Gene

- caspase recruitment domain family, member 9
- hCARD9

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CARD9 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=64170\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=64170[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CARD%5BTIAB%5D%29+OR+%28caspase+recruitment+domain+family+member+9%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+18+00+days%22%5Bdp%5D>)

Catalog of Genes and Diseases from OMIM

- CASPASE RECRUITMENT DOMAIN-CONTAINING PROTEIN 9; CARD9 (<https://omim.org/entry/607212>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/64170>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=CARD9\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=CARD9[gene]))

References

- Delsing CE, Bleeker-Rovers CP, Kullberg BJ, Netea MG. Treatment of candidiasis: insights from host genetics. *Expert Rev Anti Infect Ther.* 2012 Aug;10(8):947-56. doi: 10.1586/eri.12.79. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23030333>)
- Drewniak A, Gazendam RP, Tool AT, van Houdt M, Jansen MH, van Hamme JL, van Leeuwen EM, Roos D, Scalais E, de Beaufort C, Janssen H, van den Berg TK,

Kuijpers TW. Invasive fungal infection and impaired neutrophil killing in human CARD9 deficiency. *Blood*. 2013 Mar 28;121(13):2385-92. doi:10.1182/blood-2012-08-450551. Epub 2013 Jan 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/2335372>)

- Drummond RA, Collar AL, Swamydas M, Rodriguez CA, Lim JK, Mendez LM, Fink DL, Hsu AP, Zhai B, Karauzum H, Mikelis CM, Rose SR, Ferre EM, Yockey L, Lemberg K, Kuehn HS, Rosenzweig SD, Lin X, Chittiboina P, Datta SK, Belhorn TH, Weimer ET, Hernandez ML, Hohl TM, Kuhns DB, Lionakis MS. CARD9-Dependent Neutrophil Recruitment Protects against Fungal Invasion of the Central Nervous System. *PLoS Pathog*. 2015 Dec 17;11(12):e1005293. doi: 10.1371/journal.ppat.1005293. eCollection 2015 Dec. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/26679537>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4683065/>)
- Drummond RA, Lionakis MS. Mechanistic Insights into the Role of C-Type Lectin Receptor/CARD9 Signaling in Human Antifungal Immunity. *Front Cell Infect Microbiol*. 2016 Apr 5;6:39. doi: 10.3389/fcimb.2016.00039. eCollection 2016. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/27092298>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4820464/>)
- Engelhardt KR, Grimbacher B. Mendelian traits causing susceptibility to mucocutaneous fungal infections in human subjects. *J Allergy Clin Immunol*. 2012 Feb;129(2):294-305; quiz 306-7. doi: 10.1016/j.jaci.2011.12.966. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22284928>)
- Filler SG. Insights from human studies into the host defense against candidiasis. *Cytokine*. 2012 Apr;58(1):129-32. doi: 10.1016/j.cyto.2011.09.018. Epub 2011 Oct 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22015104>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3270114/>)
- Glocker E, Grimbacher B. Chronic mucocutaneous candidiasis and congenital susceptibility to Candida. *Curr Opin Allergy Clin Immunol*. 2010 Dec;10(6):542-50. doi: 10.1097/ACI.0b013e32833fd74f. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/20859203>)
- Lanternier F, Mahdavian SA, Barbat E, Chaussade H, Koumar Y, Levy R, Denis B, Brunel AS, Martin S, Loop M, Peeters J, de Selys A, Vanclaire J, Vermeylen C, Nassogne MC, Chatzis O, Liu L, Migaud M, Pedergnana V, Desoubeaux G, Jouvion G, Chretien F, Darazam IA, Schaffer AA, Netea MG, De Bruycker JJ, Bernard L, Reynes J, Amazrine N, Abel L, Van der Linden D, Harrison T, Picard C, Lortholary O, Mansouri D, Casanova JL, Puel A. Inherited CARD9 deficiency in otherwise healthy children and adults with Candida species-induced meningoencephalitis, colitis, or both. *J Allergy Clin Immunol*. 2015 Jun;135(6):1558-68.e2. doi:10.1016/j.jaci.2014.12.1930. Epub 2015 Feb 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25702837>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4831587/>)
- Plantinga TS, Johnson MD, Scott WK, Joosten LA, van der Meer JW, Perfect JR, Kullberg BJ, Netea MG. Human genetic susceptibility to Candida infections. *Med Mycol*. 2012 Nov;50(8):785-94. doi: 10.3109/13693786.2012.690902. Epub 2012 Jun 4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22662758>)

- Smeekens SP, van de Veerdonk FL, Kullberg BJ, Netea MG. Genetic susceptibility to Candida infections. EMBO Mol Med. 2013 Jun;5(6):805-13. doi:10.1002/emmm.201201678. Epub 2013 Apr 30. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23629947>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3779444/>)

Genomic Location

The *CARD9* gene is found on chromosome 9 (<https://medlineplus.gov/genetics/chromosome/9/>).

Last updated September 1, 2016