

MEFV gene

MEFV innate immunity regulator, pyrin

Normal Function

The *MEFV* gene provides instructions for making a protein called pyrin (also known as marenostrin). Although pyrin's function is not fully understood, it likely assists in keeping the inflammation process under control. Inflammation occurs when the immune system sends signaling molecules and white blood cells to a site of injury or disease to fight microbial invaders and facilitate tissue repair. When this has been accomplished, the body stops the inflammatory response to prevent damage to its own cells and tissues.

Pyrin is produced in certain white blood cells (neutrophils, eosinophils, and monocytes) that play a role in inflammation and in fighting infection. Pyrin may direct the migration of white blood cells to sites of inflammation and stop or slow the inflammatory response when it is no longer needed. Pyrin also interacts with other molecules to assemble themselves into structures called inflammasomes, which are involved in the process of inflammation. Research indicates that pyrin helps regulate inflammation by interacting with the cytoskeleton, the structural framework that helps to define the shape, size, and movement of a cell.

Health Conditions Related to Genetic Changes

Familial Mediterranean fever

More than 80 *MEFV* gene variants (also known as mutations) have been found to cause familial Mediterranean fever. A few variants delete small amounts of DNA from the *MEFV* gene, which can lead to an abnormally small, nonfunctional protein. Most *MEFV* gene variants, however, change one of the protein building blocks (amino acids) used to make pyrin. The most common variant replaces the amino acid methionine with the amino acid valine at protein position 694 (written as Met694Val or M694V). Among people with familial Mediterranean fever, this particular variant is also associated with an increased risk of developing amyloidosis, a complication in which abnormal protein deposits can lead to kidney failure. Some evidence suggests that normal variations in another gene, called *SAA1*, can further modify the risk of developing amyloidosis among people with the M694V change.

MEFV gene variants lead to reduced amounts of pyrin or a malformed pyrin protein that cannot function properly. As a result, pyrin cannot perform its presumed role in controlling inflammation, leading to an inappropriate or prolonged inflammatory response. Fever and inflammation in the abdomen, chest, joints, or skin are signs of familial Mediterranean fever.

Other Names for This Gene

- FMF
- marenostrin
- Mediterranean fever
- MEF
- MEFV_HUMAN
- MRST
- pyrin
- TRIM20

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of MEFV ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4210\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4210[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28MEFV%5BTIAB%5D%29+OR+%28Mediterranean+fever%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+360+days%22%5Bdp%5D%29%29%29>)

Catalog of Genes and Diseases from OMIM

- MEFV INNATE IMMUNITY REGULATOR, PYRIN; MEFV (<https://omim.org/entry/608107>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/4210>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=MEFV\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=MEFV[gene]))

References

- Aksentijevich I, Torosyan Y, Samuels J, Centola M, Pras E, Chae JJ, Oddoux C, Wood G, Azzaro MP, Palumbo G, Giustolisi R, Pras M, Ostrer H, Kastner DL. Mutation and haplotype studies of familial Mediterranean fever reveal new ancestral relationships and evidence for a high carrier frequency with reduced penetrance in the Ashkenazi Jewish population. *Am J Hum Genet.* 1999 Apr;64(4):949-62. doi: 10.1086/302327. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/10090880>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1377819/>)
- Bakkaloglu A. Familial Mediterranean fever. *Pediatr Nephrol.* 2003 Sep;18(9):853-9. doi: 10.1007/s00467-003-1185-2. Epub 2003 Jun 27. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12836090>)
- Chae JJ, Wood G, Masters SL, Richard K, Park G, Smith BJ, Kastner DL. The B30.2 domain of pyrin, the familial Mediterranean fever protein, interacts directly with caspase-1 to modulate IL-1 β production. *Proc Natl Acad Sci U S A.* 2006 Jun 27;103(26):9982-7. doi: 10.1073/pnas.0602081103. Epub 2006 Jun 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16785446>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1479864/>)
- Delibas A, Oner A, Balci B, Demircin G, Bulbul M, Bek K, Erdogan O, Baysun S, Yilmaz E. Genetic risk factors of amyloidogenesis in familial Mediterranean fever. *Am J Nephrol.* 2005 Sep-Oct;25(5):434-40. doi: 10.1159/000087824. Epub 2005 Aug 23. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16118480>)
- Gershoni-Baruch R, Brik R, Zacks N, Shinawi M, Lidar M, Livneh A. The contribution of genotypes at the MEFV and SAA1 loci to amyloidosis and disease severity in patients with familial Mediterranean fever. *Arthritis Rheum.* 2003 Apr;48(4):1149-55. doi: 10.1002/art.10944. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12687559>)
- Mansfield E, Chae JJ, Komarow HD, Brotz TM, Frucht DM, Aksentijevich I, Kastner DL. The familial Mediterranean fever protein, pyrin, associates with microtubules and colocalizes with actin filaments. *Blood.* 2001 Aug 1;98(3):851-9. doi: 10.1182/blood.v98.3.851. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11468188>)
- Medlej-Hashim M, Delague V, Chouery E, Salem N, Rawashdeh M, Lefranc G, Loiselet J, Megarbane A. Amyloidosis in familial Mediterranean fever patients: correlation with MEFV genotype and SAA1 and MICA polymorphisms effects. *BMC Med Genet.* 2004 Feb 10;5:4. doi: 10.1186/1471-2350-5-4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15018633>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC356915/>)
- Mikula M, Buller A, Sun W, Strom CM. Prevalence of known mutations in the familial Mediterranean fever gene (MEFV) in various carrier screening populations. *Genet Med.* 2008 May;10(5):349-52. doi: 10.1097/GIM.0b013e3181723cc8. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18496034>)
- Milhavet F, Cuisset L, Hoffman HM, Slim R, El-Shanti H, Aksentijevich I, Lesage S, Waterham H, Wise C, Sarrauste de Menthier C, Touitou I. The infersautoinflammatory mutation online registry: update with new genes and

functions. Hum Mutat. 2008 Jun;29(6):803-8. doi: 10.1002/humu.20720. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18409191>)

- Notarnicola C, Didelot MN, Kone-Paut I, Seguret F, Demaille J, Touitou I. Reduced MEFV messenger RNA expression in patients with familial Mediterranean fever. Arthritis Rheum. 2002 Oct;46(10):2785-93. doi: 10.1002/art.10575. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12384939>)
- Papin S, Cuenin S, Agostini L, Martinon F, Werner S, Beer HD, Grutter C, Grutter M, Tschopp J. The SPRY domain of Pyrin, mutated in familial Mediterranean fever patients, interacts with inflammasome components and inhibits proIL-1 β processing. Cell Death Differ. 2007 Aug;14(8):1457-66. doi:10.1038/sj.cdd.4402142. Epub 2007 Apr 13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17431422>)
- Rabinovitch E, Harats D, Yaron P, Luvish T, Lidar M, Kedem R, Shaish A, Ben-Dov I, Livneh A. Familial Mediterranean fever gene and protection against asthma. Ann Allergy Asthma Immunol. 2007 Dec;99(6):517-21. doi:10.1016/S1081-1206(10)60380-8. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18219832>)
- Ross JJ. Goats, germs, and fever: Are the pyrin mutations responsible for familial Mediterranean fever protective against Brucellosis? Med Hypotheses. 2007;68(3):499-501. doi: 10.1016/j.mehy.2006.07.027. Epub 2006 Sep 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17005326>)
- Stoffman N, Magal N, Shohat T, Lotan R, Koman S, Oron A, Danon Y, Halpern GJ, Lifshitz Y, Shohat M. Higher than expected carrier rates for familial Mediterranean fever in various Jewish ethnic groups. Eur J Hum Genet. 2000 Apr;8(4):307-10. doi: 10.1038/sj.ejhg.5200446. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/10854115>)
- Telatar M, Grody WW. Molecular genetic testing for familial Mediterranean fever. Mol Genet Metab. 2000 Sep-Oct;71(1-2):256-60. doi: 10.1006/mgme.2000.3047. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11001819>)
- Yepiskoposyan L, Harutyunyan A. Population genetics of familial Mediterranean fever: a review. Eur J Hum Genet. 2007 Sep;15(9):911-6. doi:10.1038/sj.ejhg.5201869. Epub 2007 Jun 13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17568393>)
- Yu JW, Fernandes-Alnemri T, Datta P, Wu J, Juliana C, Solorzano L, McCormick M, Zhang Z, Alnemri ES. Pyrin activates the ASC pyroptosome in response to engagement by autoinflammatory PSTPIP1 mutants. Mol Cell. 2007 Oct 26;28(2):214-27. doi: 10.1016/j.molcel.2007.08.029. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17964261>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2719761/>)

Genomic Location

The *MEFV* gene is found on chromosome 16 (<https://medlineplus.gov/genetics/chromosome/16/>).

Last updated August 11, 2021