NLRP3 gene

NLR family pyrin domain containing 3

Normal Function

The *NLRP3* gene provides instructions for making a protein called cryopyrin. Cryopyrin is a member of a family of proteins called intracellular "NOD-like" receptor (NLR) proteins. Cryopyrin is found mainly in white blood cells and in cartilage-forming cells (chondrocytes).

NLR proteins are involved in the immune system, helping to start and regulate the immune system's response to injury, toxins, or foreign invaders. NLR proteins recognize specific molecules and respond by helping to turn on (activate) certain parts of the immune system. Cryopyrin recognizes bacteria; chemicals such as asbestos, silica, and uric acid crystals; and compounds released by injured cells.

Cryopyrin molecules assemble themselves, along with other proteins, into structures called inflammasomes, which help trigger the process of inflammation. Inflammation occurs when the immune system sends signaling molecules as well as white blood cells to a site of injury or disease to fight foreign invaders and help repair damaged tissues. Once the threat is over, the body stops (inhibits) the inflammatory response, to prevent damage to its own cells and tissues.

Health Conditions Related to Genetic Changes

Cryopyrin-associated periodic syndromes

Several variants (also known as mutations) in the *NLRP3* gene have been found to cause cryopyrin-associated periodic syndromes (CAPS). CAPS are a group of conditions that have overlapping signs and symptoms. The conditions are generally characterized by periodic episodes of skin rash, fever, and joint pain. CAPS include three conditions known as familial cold autoinflammatory syndrome type 1 (FCAS1), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disorder (NOMID). These conditions were once thought to be distinct disorders but are now considered to be part of the same condition spectrum. FCAS1 is the least severe form of CAPS, MWS is intermediate in severity, and NOMID is the most severe form.

Many of the variants that cause CAPS are in a region of the *NLRP3* gene known as exon 3. All of the variants likely result in the cryopyrin protein being overactive.

Inflammasomes made with abnormal cryopyrin proteins trigger inflammatory responses even when there is no injury or disease. Impairment of the body's mechanisms for controlling inflammation results in episodes of fever and widespread damage to the body's cells and tissues.

While the CAPS spectrum shares similar signs and symptoms, it is unclear why variants in different parts of the *NLRP3* gene cause the patterns of features that distinguish FCAS1, MWS, and NOMID.

Other Names for This Gene

- AII/AVP
- AII/AVP receptor-like
- angiotensin/vasopressin receptor AII/AVP-like
- AVP
- C1orf7
- CIAS1
- CLR1.1
- cryopyrin
- NACHT domain-, leucine-rich repeat-, and PYD-containing protein 3
- NACHT, LRR and PYD containing protein 3
- NALP3_HUMAN
- NLR family, pyrin domain containing 3
- nucleotide-binding oligomerization domain, leucine rich repeat and pyrin domain containing 3
- PYPAF1
- PYRIN-containing APAF1-like protein 1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NLRP3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=114548[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28NLRP3%5BTIAB%5D%29+OR+%28%28AII/AVP%5BTIAB%5D%29+OR+%28CIAS1%5BTIAB%5D%29+OR+%28cryopyrin%5BTIAB%5D%29+OR+%28FCAS%5BTIAB%5D%29+OR+%28FCU%5BTIAB%5D%29+OR+%28NALP3%5BTIAB%5D%29+OR+%28PYPAF1%5BTIAB%5D%29+OR+%28PYRIN-containing+APAF1-like+protein+1%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)

Catalog of Genes and Diseases from OMIM

- NLR FAMILY, PYRIN DOMAIN-CONTAINING 3; NLRP3 (https://omim.org/entry/606416)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/114548)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=NLRP3[gene])

References

- Church LD, Cook GP, McDermott MF. Primer: inflammasomes and interleukin 1betain inflammatory disorders. Nat Clin Pract Rheumatol. 2008 Jan;4(1):34-42. doi: 10.1038/ncprheum0681. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18172447)
- Paim-Marques LB, Cavalcante A, Castro C, Muskardin TLW, de Oliveira JB, Niewold TB, Appenzeller S. Novel mutation in the NRLP3 manifesting as anintermediate phenotype of cryopyrinopathies. Rheumatol Int. 2021Jan;41(1):219-225. doi: 10.1007/s00296-020-04683-5. Epub 2020 Aug 19. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/32813153)
- Sutterwala FS, Ogura Y, Szczepanik M, Lara-Tejero M, Lichtenberger GS, GrantEP, Bertin J, Coyle AJ, Galan JE, Askenase PW, Flavell RA. Critical role forNALP3/CIAS1/Cryopyrin in innate and adaptive immunity through its regulation ofcaspase-1. Immunity. 2006 Mar;24(3):317-27. doi: 10.1016/j.immuni.2006.02.004. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16546100)
- Tunca M, Ozdogan H. Molecular and genetic characteristics of hereditaryautoinflammatory diseases. Curr Drug Targets Inflamm Allergy. 2005Feb;4(1):77-80. doi: 10.2174/1568010053622957. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15720239)
- Welzel T, Kuemmerle-Deschner JB. Diagnosis and Management of theCryopyrin-Associated Periodic Syndromes (CAPS): What Do We Know Today? J ClinMed. 2021 Jan 1;10(1):128. doi: 10.3390/jcm10010128. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/33401496)

Genomic Location

The *NLRP3* gene is found on chromosome 1 (https://medlineplus.gov/genetics/chromosome/1/).

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