NLRP12 gene

NLR family pyrin domain containing 12

Normal Function

The *NLRP12* gene provides instructions for making a protein called monarch-1. Monarch-1 is a member of a family of proteins called intracellular "NOD-like" receptor (NLR) proteins. Monarch-1 is found mainly in certain types of white blood cells.

NLR proteins are involved in the immune system, helping to control the immune system' s response to injury, toxins, or foreign invaders. The monarch-1 protein is involved in an immune process known as inflammation. Inflammation occurs when the immune system sends signaling molecules and white blood cells to a site of injury or disease to fight foreign invaders and help with tissue repair. After this has been accomplished, stopping the inflammatory response helps to prevent damage to the body's own cells and tissues.

Monarch-1 primarily stops (inhibits) inflammation by blocking the release of specific molecules that are involved in the process. However, monarch-1 can also promote the production of proteins that trigger inflammation when certain molecules are present.

Health Conditions Related to Genetic Changes

Familial cold autoinflammatory syndrome type 2

At least 20 variants (also known as mutations) in the *NLRP12* gene have been found to cause familial cold autoinflammatory syndrome type 2. This condition causes episodes of fever, skin rash, and joint pain, often in response to cold temperatures.

Many of the *NLRP12* gene variants that cause familial cold autoinflammatory syndrome type 2 are in a region of the gene known as exon 3. Most *NLRP12* gene variants appear to reduce the ability of the monarch-1 protein to inhibit inflammation, resulting in an unusually long inflammatory response. However, research shows that other variants increase the protein's ability to trigger inflammatory responses, even when there is no injury or disease.

Impairment of the body's mechanisms for controlling inflammation results in the episodes of skin rash, fever, and joint pain seen in familial cold autoinflammatory syndrome type 2. It is unclear why episodes can be triggered by cold exposure in this disorder.

Additional changes in the *NLRP12* gene or changes in other genes may influence the severity of familial cold autoinflammatory syndrome type 2, but little is known about how these changes contribute to the condition.

In some families, individuals with an *NLRP12* gene variant may develop familial cold autoinflammatory syndrome type 2 but others with the mutation do not, which is a situation known as reduced penetrance.

Other Names for This Gene

- monarch 1
- Monarch1
- NACHT, leucine rich repeat and PYD containing 12
- NACHT, LRR and PYD containing protein 12
- NALP12
- NLR family, pyrin domain containing 12
- nucleotide-binding oligomerization domain, leucine rich repeat and pyrin domain containing 12
- PAN6
- PYPAF7
- PYRIN-containing APAF1-like protein 7

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NLRP12 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=91662[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=(NLRP12%5BTI%5D))

Catalog of Genes and Diseases from OMIM

- NLR FAMILY, PYRIN DOMAIN-CONTAINING 12; NLRP12 (https://omim.org/entry/609648)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/91662)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=NLRP12[gene])

References

- Ayla AY, Eren H, Zare J, Calhan SS, Karacan I, Seven M, Ugurlu S. A rare caseof an NLRP12-associated autoinflammatory disease. Eur J Med Genet. 2021Apr;64(4): 104168. doi: 10.1016/j.ejmg.2021.104168. Epub 2021 Mar 3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/33676062)
- Del Porto F, Cifani N, Proietta M, Verrecchia E, Di Rosa R, Manna R, ChiurazziP. NLRP12 gene mutations and auto-inflammatory diseases: ever-changing evidence. Rheumatology (Oxford). 2020 Nov 1;59(11):3129-3136. doi:10.1093/rheumatology/keaa304. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/32725138)
- Gupta L, Ahmed S, Singh B, Prakash S, Phadke S, Aggarwal A. Novel NLRP12variant presenting with familial cold autoimmunity syndrome phenotype. Ann RheumDis. 2021 Jul;80(7):e117. doi: 10.1136/annrheumdis-2019-216158. Epub 2019 Aug 24.No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/31446425)
- Jeru I, Duquesnoy P, Fernandes-Alnemri T, Cochet E, Yu JW, Lackmy-Port-Lis M, Grimprel E, Landman-Parker J, Hentgen V, Marlin S, McElreavey K, Sarkisian T, Grateau G, Alnemri ES, Amselem S. Mutations in NALP12 cause hereditary periodicfever syndromes. Proc Natl Acad Sci U S A. 2008 Feb 5;105(5):1614-9. doi: 10.1073/pnas.0708616105. Epub 2008 Jan 29. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18230725) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2234193/)
- Wang W, Zhou Y, Zhong LQ, Li Z, Jian S, Tang XY, Song HM. The clinicalphenotype and genotype of NLRP12-autoinflammatory disease: a Chinese case serieswith literature review. World J Pediatr. 2020 Oct;16(5):514-519. doi:10.1007/s12519-019-00294-8. Epub 2019 Dec 9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/31820221)

Genomic Location

The *NLRP12* gene is found on chromosome 19 (https://medlineplus.gov/genetics/chromosome/19/).

Last updated August 12, 2021