

IL36RN Gene

Subjects: **Genetics & Heredity**

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Interleukin 36 receptor antagonist

genes

1. Introduction

The *IL36RN* gene provides instructions for making a protein called interleukin 36 receptor antagonist (IL-36Ra). This protein is primarily found in the skin where it helps regulate inflammation, part of the body's early immune response. Inflammation in the skin is stimulated when other proteins called IL-36 alpha (α), IL-36 beta (β), or IL-36 gamma (γ) attach to (bind) a specific receptor protein. This binding turns on (activates) signaling pathways that promote inflammation, namely the NF- κ B and MAPK pathways. To control inflammatory reactions, the IL-36Ra protein binds to the receptor protein so that IL-36 α , IL-36 β , and IL-36 γ cannot. In this way, the IL-36Ra protein blocks (antagonizes) the receptor's activity.

2. Health Conditions Related to Genetic Changes

2.1. Generalized Pustular Psoriasis

More than a dozen *IL36RN* gene mutations have been found to increase susceptibility to a serious skin disorder called generalized pustular psoriasis (GPP). Individuals with this condition have repeated episodes in which large areas of skin become red and inflamed and develop small pus-filled blisters (pustules). The skin problems can be accompanied by fever and other signs of inflammation throughout the body (systemic inflammation). The episodes are thought to be triggered by infections, certain medications, menstruation, pregnancy, or other stresses on the body.

The *IL36RN* gene mutations associated with GPP reduce the amount of IL-36Ra protein in the skin or eliminate it altogether. Without control by IL-36Ra, signaling pathways that promote inflammation are overly active, resulting in uncontrolled inflammation, particularly in the skin.

IL36RN gene mutations increase the risk of developing GPP. Not everyone with mutations in this gene has the characteristic problems with inflammation. This complex condition is thought to arise from a combination of genetic and environmental factors.

2.2. Other Disorders

IL36RN gene mutations are also associated with other inflammatory skin conditions that involve pustule formation. Like GPP (described above), acute generalized exanthematous pustulosis (AGEP), is characterized by a rash and pustules over a large area of the body, typically triggered by antibiotics or other medications. (Certain features of the inflamed skin differentiate AGEP and GPP.) Other *IL36RN*-associated conditions are classified as forms of localized pustular psoriasis because the blisters are found in limited regions of the body. For example, palmoplantar pustulosis affects the hands and feet, and acrodermatitis continua of Hallopeau affects the tips of the fingers and toes. It is unclear how mutations in the same gene cause these different conditions.

IL36RN gene mutations have been found in individuals with a condition called geographic tongue, in which the top and sides of the tongue have irregular patches that resemble a map. The patches are not linked to infections or other health problems. Some people with GPP have geographic tongue, but the abnormality can also occur without features of other conditions.

3. Other Names for This Gene

- FIL1
- FIL1(Delta)
- FIL1D
- IL-1 related protein 3
- IL-1F5
- IL-36Ra
- IL1F5
- IL1HY1
- IL1L1
- IL1RP3
- IL36RA
- interleukin 1 family, member 5 (delta)
- interleukin-1 HY1

- interleukin-1 receptor antagonist homolog 1
- interleukin-1-like protein 1
- interleukin-36 receptor antagonist protein
- MGC29840
- PSORP
- PSORS14

References

1. Farooq M, Nakai H, Fujimoto A, Fujikawa H, Matsuyama A, Kariya N, Aizawa A, Fujiwara H, Ito M, Shimomura Y. Mutation analysis of the IL36RN gene in 14 Japanese patients with generalized pustular psoriasis. *Hum Mutat.* 2013 Jan;34(1):176-83. doi: 10.1002/humu.22203.
2. Hussain S, Berki DM, Choon SE, Burden AD, Allen MH, Arostegui JI, Chaves A, Duckworth M, Irvine AD, Mockenhaupt M, Navarini AA, Seyger MM, Soler-Palacin P, Prins C, Valeyrie-Allanore L, Vicente MA, Trembath RC, Smith CH, Barker JN, Capon F. IL36RN mutations define a severe autoinflammatory phenotype of generalized pustular psoriasis. *J Allergy Clin Immunol.* 2015 Apr;135(4):1067-70.e9. doi:10.1016/j.jaci.2014.09.043.
3. Kardaun SH, Kuiper H, Fidler V, Jonkman MF. The histopathological spectrum of acute generalized exanthematous pustulosis (AGEP) and its differentiation from generalized pustular psoriasis. *J Cutan Pathol.* 2010 Dec;37(12):1220-9. doi:10.1111/j.1600-0560.2010.01612.x.
4. Körber A, Mössner R, Renner R, Sticht H, Wilschmann-Theis D, Schulz P, Sticherling M, Traupe H, Hüffmeier U. Mutations in IL36RN in patients with generalized pustular psoriasis. *J Invest Dermatol.* 2013 Nov;133(11):2634-2637. doi: 10.1038/jid.2013.214.
5. Liang J, Huang P, Li H, Zhang J, Ni C, Wang Y, Shen J, Li C, Kang L, Chen J, Zhang H, Wang Z, Zhang Z, Li M, Yao Z. Mutations in IL36RN are associated with geographic tongue. *Hum Genet.* 2017 Feb;136(2):241-252. doi:10.1007/s00439-016-1750-y.
6. Onoufriadis A, Simpson MA, Pink AE, Di Meglio P, Smith CH, Pullabhatla V, Knight J, Spain SL, Nestle FO, Burden AD, Capon F, Trembath RC, Barker JN. Mutations in IL36RN/IL1F5 are associated with the severe episodic inflammatory skin disease known as generalized pustular psoriasis. *Am J Hum Genet.* 2011 Sep 9;89(3):432-7. doi: 10.1016/j.ajhg.2011.07.022.
7. Setta-Kaffetzi N, Navarini AA, Patel VM, Pullabhatla V, Pink AE, Choon SE, Allen MA, Burden AD, Griffiths CE, Seyger MM, Kirby B, Trembath RC, Simpson MA, Smith CH, Capon F, Barker JN.

Rare pathogenic variants in IL36RN underlie aspectrum of psoriasis-associated pustular phenotypes. *J Invest Dermatol.* 2013May;133(5):1366-9. doi: 10.1038/jid.2012.490.

8. Tauber M, Bal E, Pei XY, Madrange M, Khelil A, Sahel H, Zenati A, Makrelouf M, Boubridaa K, Chiali A, Smahi N, Otsmane F, Bouajar B, Marrakchi S, Turki H, Bourrat E, Viguier M, Hamel Y, Bachelez H, Smahi A. IL36RN Mutations Affect Protein Expression and Function: A Basis for Genotype-Phenotype Correlation in Pustular Diseases. *J Invest Dermatol.* 2016 Sep;136(9):1811-1819. doi:10.1016/j.jid.2016.04.038.

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