SPINK5 Gene

Subjects: Genetics & Heredity
Contributor: Karina Chen

serine peptidase inhibitor, Kazal type 5

Keywords: genes

1. Normal Function

The *SPINK5* gene provides instructions for making a protein called LEKT1. LEKT1 is a type of serine peptidase inhibitor. Serine peptidase inhibitors control the activity of enzymes called serine peptidases, which break down other proteins. LEKT1 is found in the skin and in the thymus, which is a gland located behind the breastbone that plays an important role in the immune system by producing white blood cells called lymphocytes. LEKT1 controls the activity of certain serine peptidases in the outer layer of skin (the epidermis), especially the tough outer surface known as the stratum corneum, which provides a sturdy barrier between the body and its environment. Serine peptidase enzymes are involved in normal skin shedding by helping to break the connections between cells of the stratum corneum. LEKT1 is also involved in normal hair growth, the development of lymphocytes in the thymus, and the control of peptidases that trigger immune system function.

2. Health Conditions Related to Genetic Changes

2.1. Netherton syndrome

At least 70 *SPINK5* gene mutations have been identified in people with Netherton syndrome, a disorder involving skin and hair abnormalities and a high risk of allergies, asthma, and an inflammatory skin condition called eczema. Mutations in the *SPINK5* gene result in a LEKT1 protein that is unable to control serine peptidase activity. The lack of LEKT1 function allows the serine peptidases to be abnormally active and break down too many proteins in the stratum corneum. As a result, excessive skin shedding takes place, and the stratum corneum is unusually thin and breaks down easily, resulting in the skin abnormalities that occur in Netherton syndrome. Loss of LEKT1 function also results in abnormal hair growth. The immune dysfunction that leads to allergies, asthma, and eczema in people with Netherton syndrome likely arises from a lack of LEKT1 control of peptidases involved in the triggering of immune system function. Excessive activation of the immune system caused by invasion of microbes in the abnormal skin is also thought to be involved.

2.2. Other disorders

Normal variations (polymorphisms) in the *SPINK5* gene have been associated with an increased risk of abnormal triggering (hypersensitivity) of the immune system, known as atopy. Atopy leads to disorders such as allergies, eczema, and asthma. *SPINK5* gene variations may affect the ability of LEKT1 to control peptidases involved in triggering the immune system, leading to an increased risk of these disorders.

3. Other Names for This Gene

- DKFZp686K19184
- FLJ21544
- FLJ97536
- FLJ97596
- FLJ99794
- ISK5_HUMAN
- LEKTI
- LETKI
- lympho-epithelial Kazal-type-related inhibitor

- lymphoepithelial Kazal-type-related inhibitor
- NETS
- NS
- serine protease inhibitor Kazal-type 5
- serine protease inhibitor, Kazal type 5
- VAKTI

References

1. Bitoun E, Chavanas S, Irvine AD, Lonie L, Bodemer C, Paradisi M, Hamel-TeillacD, Ansai S, Mitsuhashi Y, Taïeb A, de Prost Y, Zambruno G, Harper JI, HovnanianA. Netherton syndrome: disease expression and spectrum of SPINK5 mutations in 21 families. J Invest Dermatol. 2002 Feb;118(2):352-61.
2. D'Alessio M, Fortugno P, Zambruno G, Hovnanian A. Netherton syndrome and itsmultifaceted defective protein LEKTI. G Ital Dermatol Venereol. 2013Feb;148(1):37-51. Review.
3. Hovnanian A. Netherton syndrome: skin inflammation and allergy by loss ofprotease inhibition. Cell Tissue Res. 2013 Feb;351(2):289-300. doi:10.1007/s00441-013-1558-1.
4. Lacroix M, Lacaze-Buzy L, Furio L, Tron E, Valari M, Van der Wier G, BodemerC, Bygum A, Bursztejn AC, Gaitanis G, Paradisi M, Stratigos A, Weibel L, DeraisonC, Hovnanian A. Clinical expression and new SPINK5 splicing defects in Netherton syndrome: unmasking a frequent founder synonymous mutation and unconventionalintronic mutations. J Invest Dermatol. 2012 Mar;132(3 Pt 1):575-82. doi:10.1038/jid.2011.366.
5. Liu Q, Xia Y, Zhang W, Li J, Wang P, Li H, Wei C, Gong Y. A functionalpolymorphism in the SPINK5 gene is associated with asthma in a Chinese HanPopulation. BMC Med Genet. 2009 Jun 17;10:59. doi: 10.1186/1471-2350-10-59.
6. Roelandt T, Thys B, Heughebaert C, De Vroede A, De Paepe K, Roseeuw D, RombautB, Hachem JP. LEKTI-1 in sickness and in health. Int J Cosmet Sci. 2009Aug;31(4):247-54. doi: 10.1111/j.1468-2494.2009.00516.x.Review.
7. Sprecher E, Chavanas S, DiGiovanna JJ, Amin S, Nielsen K, Prendiville JS,Silverman R, Esterly NB, Spraker MK, Guelig E, de Luna ML, Williams ML, BuehlerB, Siegfried EC, Van Maldergem L, Pfendner E, Bale SJ, Uitto J, Hovnanian A,Richard G. The spectrum of pathogenic mutations in SPINK5 in 19 families withNetherton syndrome: implications for mutation detection and first case ofprenatal diagnosis. J Invest Dermatol. 2001 Aug;117(2):179-87.
8. Zhao LP, Di Z, Zhang L, Wang L, Ma L, Lv Y, Hong Y, Wei H, Chen HD, Gao XH.Association of SPINK5 gene polymorphisms with atopic dermatitis in NortheastChina. J Eur Acad Dermatol Venereol. 2012 May;26(5):572-7. doi:10.1111/j.1468-3083.2011.04120.x.