LAMA3 gene

laminin subunit alpha 3

Normal Function

The *LAMA3* gene provides instructions for making one part (subunit) of a protein called laminin 332 (formerly known as laminin 5). This protein is made up of three subunits, called alpha, beta, and gamma. The *LAMA3* gene carries instructions for the alpha subunit; the beta and gamma subunits are produced from other genes. Three versions of the alpha subunit, called alpha-3a, alpha-3b1, and alpha-3b2, are produced from the *LAMA3* gene.

Laminins are a group of proteins that regulate cell growth, cell movement (motility), and the attachment of cells to one another (adhesion). They are also involved in the formation and organization of basement membranes, which are thin, sheet-like structures that separate and support cells in many tissues. Laminin 332 has a particularly important role in the basement membrane that underlies the top layer of skin (the epidermis). This membrane gives strength and resiliency to the skin and creates an additional barrier between the body and its surrounding environment. Laminin 332 is a major component of fibers called anchoring filaments, which connect the two layers of the basement membrane and help hold the skin together.

Studies suggest that laminin 332 also has several other functions. This protein appears to be important in the formation of early wound-healing tissues. Additionally, researchers have proposed roles for laminin 332 in the clear outer covering of the eye (the cornea) and in the development of tooth enamel.

The alpha subunit produced from the *LAMA3* gene is also part of two other laminin proteins, laminin 311 and laminin 321. These laminins also appear to provide strength to the skin, although they do not play as big a role as laminin 332. In addition, laminin 311 is involved in cell signaling in the lungs and other tissues.

Health Conditions Related to Genetic Changes

Junctional epidermolysis bullosa

At least 50 mutations in the *LAMA3* gene have been identified in people with junctional epidermolysis bullosa (JEB). The more serious form of the disease, known as JEB generalized severe, usually results from mutations that prevent the production of

functional laminin 332. Most of these mutations lead to a premature stop signal in the instructions for making all three versions of the alpha subunit, which disrupts the assembly of laminin 332. Without functional laminin 332, the epidermis is only weakly connected to the underlying layers of skin. Friction or other minor trauma (such as rubbing or scratching) can cause the skin layers to separate, leading to the formation of blisters. Infants with JEB generalized severe develop widespread blistering that causes life-threatening complications.

Other *LAMA3* gene mutations cause the milder form of junctional epidermolysis bullosa, JEB generalized intermediate. Some of these mutations alter single protein building blocks (amino acids) in the alpha subunit of laminin 332. Others add or remove a small number of amino acids in the alpha subunit or change the way the gene's instructions are used to make the subunit. The genetic changes responsible for milder cases of junctional epidermolysis bullosa usually lead to the production of a laminin 332 protein that retains some of its function. Affected individuals experience blistering, but it may be limited to the hands, feet, knees, and elbows.

Laryngo-onycho-cutaneous syndrome

At least three mutations in the *LAMA3* gene have been found to cause laryngo-onycho-cutaneous (LOC) syndrome. This rare disorder is characterized by chronic skin sores (ulcers) and the widespread formation of red, bumpy patches called granulation tissue. A buildup of granulation tissue in different parts of the body can lead to serious complications, including vision loss and blockage of the airway. Other features of LOC syndrome include malformed nails and abnormal teeth.

The mutations involved in LOC syndrome lead to an abnormally short version of the alpha-3a subunit of laminin 332; alpha-3b1 and alpha-3b2 are normal. Laminin proteins containing the altered alpha subunit cannot effectively attach the epidermis to underlying layers of skin or regulate wound healing. These abnormalities of laminin 332 cause the chronic skin ulceration and overgrowth of granulation tissue that are characteristic of LOC syndrome. The inability of laminin 332 to perform its other functions leads to the nail and tooth abnormalities that occur in this condition.

LOC syndrome is typically considered a subtype of junctional epidermolysis bullosa (described above). Researchers suggest that *LAMA3* gene mutations that affect only the alpha-3a version of the alpha subunit lead to LOC syndrome, while mutations that also affect the other versions of the alpha subunit lead to junctional epidermolysis bullosa.

Other Names for This Gene

- BM600
- BM600 150kD subunit
- BM600-150kDa
- E170
- epiligrin
- epiligrin 170 kda subunit

- epiligrin alpha 3 subunit
- kalinin 165kD subunit
- kalinin-165kDa
- LAM5, alpha-3 subunit
- LAMA3_HUMAN
- lama3a
- laminin 5, alpha-3 subunit
- laminin A3
- laminin alpha 3
- laminin alpha 3 subunit
- laminin, alpha 3
- laminin, alpha-3
- laminin-5 alpha 3 chain
- LAMNA
- LOCS
- nicein 150kD subunit
- nicein-150kDa

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of LAMA3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3909[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28LAMA3%5BTIAB%5D%29+OR+%28laminin+%5Btiab%5D+AND+alpha+3+%5Btiab%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2160+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- LAMININ, ALPHA-3; LAMA3 (https://omim.org/entry/600805)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3909)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=LAMA3[gene])

References

- Aumailley M, Bruckner-Tuderman L, Carter WG, Deutzmann R, Edgar D, Ekblom P, Engel J, Engvall E, Hohenester E, Jones JC, Kleinman HK, Marinkovich MP, MartinGR, Mayer U, Meneguzzi G, Miner JH, Miyazaki K, Patarroyo M, Paulsson M, QuarantaV, Sanes JR, Sasaki T, Sekiguchi K, Sorokin LM, Talts JF, Tryggvason K, Uitto J,Virtanen I, von der Mark K, Wewer UM, Yamada Y, Yurchenco PD. A simplifiedlaminin nomenclature. Matrix Biol. 2005 Aug;24(5):326-32. doi:10.1016/j.matbio.2005.05.006. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15979864)
- Barzegar M, Mozafari N, Kariminejad A, Asadikani Z, Ozoemena L, McGrath JA. Anew homozygous nonsense mutation in LAMA3A underlying laryngo-onycho-cutaneoussyndrome. Br J Dermatol. 2013 Dec;169(6):1353-6. doi: 10.1111/bjd.12522. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23869449)
- Hamill KJ, McLean WH. The alpha-3 polypeptide chain of laminin 5: insight intowound healing responses from the study of genodermatoses. Clin Exp Dermatol. 2005Jul;30(4):398-404. doi: 10.1111/j.1365-2230.2005.01842.x. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15953081)
- Hamill KJ, Paller AS, Jones JC. Adhesion and migration, the diverse functionsof the laminin alpha3 subunit. Dermatol Clin. 2010 Jan;28(1):79-87. doi:10.1016/j.det.2009.10.009. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19945619) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2814596/)
- Hartwig B, Borm B, Schneider H, Arin MJ, Kirfel G, Herzog V.Laminin-5-deficient human keratinocytes: defective adhesion results in asaltatory and inefficient mode of migration. Exp Cell Res. 2007 May1;313(8):1575-87. doi: 10.1016/j.yexcr.2007.02.003. Epub 2007 Feb 9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17335805)
- Kim CC, Liang MG, Pfendner E, Kimonis VE. What syndrome is this?Laryngo-onycho-cutaneous syndrome. Pediatr Dermatol. 2007 May-Jun;24(3):306-8.doi: 10.1111/j.1525-1470.2007.00408.x. No abstract available. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17542886)
- McLean WH, Irvine AD, Hamill KJ, Whittock NV, Coleman-Campbell CM, MellerioJE, Ashton GS, Dopping-Hepenstal PJ, Eady RA, Jamil T, Phillips R, Shabbir SG,Haroon TS, Khurshid K, Moore JE, Page B, Darling J, Atherton DJ, Van Steensel MA,Munro CS, Smith FJ, McGrath JA. An unusual N-terminal deletion of the lamininalpha3a isoform leads to the chronic granulation tissue disorderlaryngo-onycho-cutaneous syndrome. Hum Mol Genet. 2003 Sep 15;12(18):2395-409.doi: 10.1093/hmg/ddg234. Epub 2003 Jul 15. Erratum In: Hum Mol Genet. 2004 Feb1;13(3):365. Phillips Rodney J [corrected to Phillips Roderic J]. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12915477)
- Nakano A, Chao SC, Pulkkinen L, Murrell D, Bruckner-Tuderman L, Pfendner E, Uitto J. Laminin 5 mutations in junctional epidermolysis bullosa: molecular basisof Herlitz vs. non-Herlitz phenotypes. Hum Genet. 2002 Jan;110(1):41-51. doi:10.1007/s00439-001-0630-1. Epub 2001 Nov 13. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11810295)

- Schneider H, Muhle C, Pacho F. Biological function of laminin-5 and pathogenicimpact of its deficiency. Eur J Cell Biol. 2007 Dec;86(11-12):701-17. doi: 10.1016/j.ejcb.2006.07.004. Epub 2006 Sep 26. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17000025)
- Varki R, Sadowski S, Pfendner E, Uitto J. Epidermolysis bullosa. I. Moleculargenetics of the junctional and hemidesmosomal variants. J Med Genet. 2006Aug;43(8):641-52. doi: 10.1136/jmg.2005.039685. Epub 2006 Feb 10. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16473856) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2564586/)

Genomic Location

The *LAMA3* gene is found on chromosome 18 (https://medlineplus.gov/genetics/chromosome/18/).

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