GJB3 Gene

Subjects: Genetics & Heredity
Contributor: Vivi Li

Gap junction protein beta 3

Keywords: genes

1. Normal Function

The *GJB3* gene provides instructions for making a protein called gap junction beta 3, more commonly known as connexin 31. This protein is part of the connexin family, a group of proteins that form channels called gap junctions on the surface of cells. Gap junctions open and close to regulate the flow of nutrients, charged atoms (ions), and other signaling molecules from one cell to another. They are essential for direct communication between neighboring cells.

Connexin 31 is found in several different parts of the body, including the outermost layer of the skin (the epidermis) and structures of the inner ear. Connexin 31 plays a role in the growth and maturation of cells in the epidermis. The exact role of this protein in the inner ear is less clear, although it appears to be involved in hearing.

2. Health Conditions Related to Genetic Changes

2.1 Erythrokeratodermia Variabilis Et Progressiva

At least 15 *GJB3* gene mutations have been identified in people with erythrokeratodermia variabilis et progressiva (EKVP), a skin disorder characterized by areas of hyperkeratosis, which is abnormally thickened skin, and temporarily reddened patches called erythematous areas. Each of these mutations changes a single protein building block (amino acid) in connexin 31. Studies suggest that the abnormal protein produced from certain *GJB3* gene mutations can build up in a cell structure called the endoplasmic reticulum (ER), triggering a harmful process known as ER stress. Researchers suspect that ER stress damages cells in the epidermis and leads to their premature death. Other *GJB3* gene mutations result in the production of abnormal proteins that may form channels that do not function properly, which may also lead to premature cell death in the epidermis. In addition, abnormal connexin 31 proteins may interact with other connexin proteins, preventing the formation or function of other types of gap junctions. The mechanisms by which epidermal damage and cell death contribute to hyperkeratosis and erythematous areas are poorly understood.

2.2 Nonsyndromic Hearing Loss

3. Other Names for This Gene

- connexin 31
- CX31
- CXB3_HUMAN
- DFNA2
- gap junction protein, beta 3, 31kDa
- PNHI

References

1. Chi J, Li L, Liu M, Tan J, Tang C, Pan Q, Wang D, Zhang Z. Pathogenicconnexin-31 forms constitutively active hemichannels to promote necrotic celldeath. PLoS One. 2012;7(2):e32531. doi: 10.1371/journal.pone.0032531.
2. Diestel S, Richard G, Döring B, Traub O. Expression of a connexin31 mutationcausing erythrokeratodermia variabilis is lethal for HeLa cells. Biochem Biophys Res Commun. 2002 Aug 23;296(3):721-8.
3. Easton JA, Albuloushi AK, Kamps MAF, Brouns GHMR, Broers JLV, Coull BJ, Oji V,van Geel M, van Steensel MAM, Martin PE. A rare missense mutation in GJB3(Cx31G45E) is associated with a unique cellular phenotype resulting in necroticcell death. Exp Dermatol. 2019 Oct;28(10):1106-1113. doi: 10.1111/exd.13542.
4. Liu XZ, Xia XJ, Xu LR, Pandya A, Liang CY, Blanton SH, Brown SD, Steel KP,Nance WE. Mutations in connexin31 underlie recessive as well as dominantnon-syndromic hearing loss. Hum Mol Genet. 2000 Jan 1;9(1):63-7.
5. Oh SK, Choi SY, Yu SH, Lee KY, Hong JH, Hur SW, Kim SJ, Jeon CJ, Kim UK.Evaluation of the pathogenicity of GJB3 and GJB6 variants associated withnonsyndromic hearing loss. Biochim Biophys Acta. 2013 Jan;1832(1):285-91. doi:10.1016/j.bbadis.2012.05.009.
6. Petersen MB, Willems PJ. Non-syndromic, autosomal-recessive deafness. ClinGenet. 2006 May;69(5):371-92. Review.
7. Richard G, Smith LE, Bailey RA, Itin P, Hohl D, Epstein EH Jr, DiGiovanna JJ, Compton JG, Bale SJ. Mutations in the human connexin gene GJB3 causeerythrokeratodermia variabilis. Nat Genet. 1998 Dec;20(4):366-9.
8. Scott CA, O'Toole EA, Mohungoo MJ, Messenger A, Kelsell DP. Novel andrecurrent connexin 30.3 and connexin 31 mutations associated witherythrokeratoderma variabilis. Clin Exp Dermatol. 2011 Jan;36(1):88-90.
9. Sugiura K, Arima M, Matsunaga K, Akiyama M. The novel GJB3 mutationp.Thr202Asn in the M4 transmembrane domain underlies erythrokeratodermiavariabilis. Br J Dermatol. 2015 Jul;173(1):309-11. doi: 10.1111/bjd.13641.
10. Xia JH, Liu CY, Tang BS, Pan Q, Huang L, Dai HP, Zhang BR, Xie W, Hu DX, ZhengD, Shi XL, Wang DA, Xia K, Yu KP, Liao XD, Feng Y, Yang YF, Xiao JY, Xie DH,Huang JZ. Mutations in the gene encoding gap junction protein beta-3 associatedwith autosomal dominant hearing impairment. Nat Genet. 1998 Dec;20(4):370-3.Erratum in: Nat Genet 1999 Feb;21(2):241.
