

## ITGB4 gene

integrin subunit beta 4

### Normal Function

The *ITGB4* gene provides instructions for making one part (the  $\beta 4$  subunit) of a protein known as an integrin. Integrins are a group of proteins that regulate the attachment of cells to one another (cell-cell adhesion) and to the surrounding network of proteins and other molecules (cell-matrix adhesion). Integrins also transmit chemical signals that regulate cell growth and the activity of certain genes.

The integrin protein made with the  $\beta 4$  subunit is known as  $\alpha 6\beta 4$  integrin. This protein is found primarily in epithelial cells, which are cells that line the surfaces and cavities of the body. The  $\alpha 6\beta 4$  integrin protein plays a particularly important role in strengthening and stabilizing the skin. It is a component of hemidesmosomes, which are microscopic structures that anchor the outer layer of the skin (the epidermis) to underlying layers. As part of a complex network of proteins in hemidesmosomes,  $\alpha 6\beta 4$  integrin helps to hold the layers of skin together.

### Health Conditions Related to Genetic Changes

#### Epidermolysis bullosa with pyloric atresia

At least 60 mutations in the *ITGB4* gene have been found to cause epidermolysis bullosa with pyloric atresia (EB-PA). In addition to skin blistering, people with EB-PA are born with a life-threatening obstruction of the digestive tract called pyloric atresia. Mutations in the *ITGB4* gene account for about 80 percent of all cases of EB-PA.

*ITGB4* gene mutations alter the normal structure and function of the  $\beta 4$  integrin subunit or prevent cells from producing enough of this subunit. As a result,  $\alpha 6\beta 4$  integrin is defective or missing. Mutations that lead to a complete or near-complete loss of  $\alpha 6\beta 4$  integrin tend to cause more severe signs and symptoms of EB-PA, while mutations that alter the structure or stability of this protein usually cause milder signs and symptoms. A shortage of functional  $\alpha 6\beta 4$  integrin causes cells in the epidermis to be fragile and easily damaged. Friction or other minor trauma can cause the skin layers to separate, leading to the widespread formation of blisters. It is less clear how mutations in the *ITGB4* gene are related to pyloric atresia.

#### Junctional epidermolysis bullosa

MedlinePlus Genetics provides information about Junctional epidermolysis bullosa

## Cancers

Researchers believe that  $\alpha 6\beta 4$  integrin may play a critical role in the progression of cancerous tumors called carcinomas. These cancers arise in epithelial cells and can affect many tissues and organs, including the breast, lung, liver, colon, and skin.

Changes in the location and activity of  $\alpha 6\beta 4$  integrin within cancer cells are associated with the progression of carcinomas. The integrin protein activates key signaling molecules, which trigger cancer cells to migrate through the body and invade other tissues. These signals also make cancer cells more resistant to self-destruction (apoptosis).

Recent studies suggest that, in addition to its role in the progression of existing carcinomas,  $\alpha 6\beta 4$  integrin may be involved in the initial formation of these tumors.

## **Other Names for This Gene**

- CD104
- CD104 antigen
- GP150
- integrin beta 4
- Integrin beta(4)
- integrin beta-4 subunit
- Integrin beta4
- integrin, beta 4
- integrin, beta-4
- ITB4\_HUMAN
- Lymphocyte antigen CD104

## **Additional Information & Resources**

### Tests Listed in the Genetic Testing Registry

- Tests of ITGB4 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3691\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3691[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ITGB4%5BTIAB%5D%29+OR+%28integrin+%5Btiab%5D+AND+beta+4+%5Btiab%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22>)

%5Bdp%5D)

### Catalog of Genes and Diseases from OMIM

- INTEGRIN, BETA-4; ITGB4 (<https://omim.org/entry/147557>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/3691>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=ITGB4\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=ITGB4[gene]))

### **References**

- Ashton GH, Sorelli P, Mellerio JE, Keane FM, Eady RA, McGrath JA. Alpha 6 beta4 integrin abnormalities in junctional epidermolysis bullosa with pyloric atresia. *Br J Dermatol*. 2001 Feb;144(2):408-14. doi:10.1046/j.1365-2133.2001.04038.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11251584>)
- Dang N, Klingberg S, Rubin AI, Edwards M, Borelli S, Relic J, Marr P, Tran K, Turner A, Smith N, Murrell DF. Differential expression of pyloric atresia in junctional epidermolysis bullosa with ITGB4 mutations suggests that pyloric atresia is due to factors other than the mutations and not predictive of a poor outcome: three novel mutations and a review of the literature. *Acta Derm Venereol*. 2008;88(5):438-48. doi: 10.2340/00015555-0484. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18779879>)
- Guo W, Pylyayeva Y, Pepe A, Yoshioka T, Muller WJ, Inghirami G, Giancotti FG. Beta 4 integrin amplifies ErbB2 signaling to promote mammary tumorigenesis. *Cell*. 2006 Aug 11;126(3):489-502. doi: 10.1016/j.cell.2006.05.047. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16901783>)
- Lipscomb EA, Mercurio AM. Mobilization and activation of a signaling competent alpha6beta4 integrin underlies its contribution to carcinoma progression. *Cancer Metastasis Rev*. 2005 Sep;24(3):413-23. doi: 10.1007/s10555-005-5133-4. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16258729>)
- Nakano A, Pulkkinen L, Murrell D, Rico J, Lucky AW, Garzon M, Stevens CA, Robertson S, Pfendner E, Uitto J. Epidermolysis bullosa with congenital pyloric atresia: novel mutations in the beta 4 integrin gene (ITGB4) and genotype/phenotype correlations. *Pediatr Res*. 2001 May;49(5):618-26. doi:10.1203/00006450-200105000-00003. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11328943>)
- Pulkkinen L, Kim DU, Uitto J. Epidermolysis bullosa with pyloric atresia: novel mutations in the beta4 integrin gene (ITGB4). *Am J Pathol*. 1998 Jan;152(1):157-66. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9422533>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1858138/>)
- Pulkkinen L, Rouan F, Bruckner-Tuderman L, Wallerstein R, Garzon M, Brown T,

Smith L, Carter W, Uitto J. Novel ITGB4 mutations in lethal and nonlethal variants of epidermolysis bullosa with pyloric atresia: missense versus nonsense. *Am J Hum Genet.* 1998 Nov;63(5):1376-87. doi: 10.1086/302116. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9792864>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1377547/>)

- Yoon SO, Shin S, Lipscomb EA. A novel mechanism for integrin-mediated ras activation in breast carcinoma cells: the alpha6beta4 integrin regulates ErbB2 translation and transactivates epidermal growth factor receptor/ErbB2 signaling. *Cancer Res.* 2006 Mar 1;66(5):2732-9. doi: 10.1158/0008-5472.CAN-05-2941. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16510594>)

## Genomic Location

The *ITGB4* gene is found on chromosome 17 (<https://medlineplus.gov/genetics/chromosome/17/>).

**Last updated September 1, 2009**