ITGB4 gene
integrin subunit beta 4

Normal Function

The *ITGB4* gene provides instructions for making one part (the β4 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 β4 subunit is known as α6β4 integrin. This protein is found primarily in epithelial cells, which are cells that line the surfaces and cavities of the body. The α6β4 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, α6β4 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 β4 integrin subunit or prevent cells from producing enough of this subunit. As a result, α6β4 integrin is defective or missing. Mutations that lead to a complete or near-complete loss of α6β4 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 α6β4 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
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.

Chromosomal Location

Cytogenetic Location: 17q25.1, which is the long (q) arm of chromosome 17 at position 25.1

Molecular Location: base pairs 75,721,339 to 75,757,819 on chromosome 17 (Homo sapiens Updated Annotation Release 109.20200228, GRCh38.p13) (NCBI)

Other Names for This Gene

- CD104
- CD104 antigen
- GP150
- integrin beta 4
- integrin beta-4 subunit
- Integrin beta(4)
- Integrin beta4
- integrin, beta-4
- integrin, beta 4
• ITB4_HUMAN
• Lymphocyte antigen CD104

Additional Information & Resources

Educational Resources
• Madame Curie Bioscience Database: Integrins in Cancer Cell Invasion
  https://www.ncbi.nlm.nih.gov/books/NBK6070/
• Madame Curie Bioscience Database: Integrins: An Overview of Structural and Functional Aspects
  https://www.ncbi.nlm.nih.gov/books/NBK6259/
• Molecular Biology of the Cell (fourth edition, 2002): Integrins
  https://www.ncbi.nlm.nih.gov/books/NBK26867/

Clinical Information from GeneReviews
• Epidermolysis Bullosa with Pyloric Atresia
  https://www.ncbi.nlm.nih.gov/books/NBK1157

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?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%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5D+AND+human%5Bmh%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5D

Catalog of Genes and Diseases from OMIM
• INTEGRIN, BETA-4
  http://omim.org/entry/147557

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ITGB4.html
• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ITGB4%5Bgene%5D
• HGNC Gene Symbol Report
• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3691
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11251584

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18779879

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16901783

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16258729

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11328943

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9422533
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1858138/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9792864
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1377547/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16510594

Reprinted from Genetics Home Reference: