# ITGB3 Gene

Subjects: Genetics & Heredity
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Integrin subunit beta 3

Keywords: genes

## 1. Intrduction

The *ITGB3* gene provides instructions for making the beta3 subunit of a receptor protein called integrin alphaIIb/beta3 (αIIbβ3), which is found on the surface of small cells called platelets. Platelets circulate in blood and are an essential component of blood clots. The beta3 subunit attaches (binds) to the alphaIIb subunit, which is produced from the *ITGA2B* gene, to form integrin αIIbβ3. It is estimated that 80,000 to 100,000 copies of integrin αIIbβ3 are present on the surface of each platelet.

During clot formation, integrin αIIbβ3 binds to a protein called fibrinogen. Attachment of integrin αIIbβ3 from adjacent platelets to the same fibrinogen protein helps platelets cluster together (platelet cohesion) to form a blood clot. Blood clots protect the body after injury by sealing off damaged blood vessels and preventing further blood loss. Integrin αIIbβ3 can also bind other proteins on platelets and in the blood as well as proteins within the intricate lattice that forms in the space between cells (extracellular matrix) to ensure proper clot formation and promote wound healing.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Glanzmann Thrombasthenia

At least 130 mutations in the *ITGB3* gene have been found to cause Glanzmann thrombasthenia, which is a rare bleeding disorder. The mutations that cause this disorder occur in both copies of the gene in each cell and impair the production or activity of the beta3 subunit, which disrupts the formation of functional integrin αIIbβ3. A shortage (deficiency) of functional integrin αIIbβ3 prevents sufficient binding of fibrinogen or other proteins, impairing the formation of blood clots. A lack of platelet cohesion leads to prolonged or spontaneous bleeding episodes experienced by people with Glanzmann thrombasthenia.

### 2.2. Other Disorders

Mutations in the *ITGB3* gene can also cause another rare bleeding disorder called platelet-type bleeding disorder 16. People with this disorder have signs and symptoms similar to Glanzmann thrombasthenia (described above), including frequent nosebleeds (epistaxis), bleeding from the gums, or red or purple spots on the skin caused by bleeding underneath the skin (petechiae), but the episodes are typically milder.

Unlike Glanzmann thrombasthenia, this disorder results from a mutation in only one copy of the *ITGB3* gene in each cell, and the mutations result in the formation of some integrin αIIbβ3 that is abnormally turned on (active), even when no clot is being formed. This abnormally active protein is unable to reach the surface of the platelet where it is needed to bind to other platelets during clot formation. The overactive integrin αIIbβ3 binds inappropriately to clotting proteins within the cell during the formation of platelets, causing the platelets to become misshapen and large. The abnormally shaped platelets have a shortened lifespan, so platelet numbers are often reduced, which impairs clot formation. (The combination of reduced numbers of enlarged platelets is referred to as macrothrombocytopenia.)

Because the mutation that causes this disorder affects only one copy of the *ITGB3* gene, some normal integrin is formed and normal platelets produced, which accounts for the mild signs and symptoms in affected individuals.

## 3. Other Names for This Gene

- beta 3 integrin
- CD61
- GP3A
- GPIIIa
- integrin beta 3
- integrin beta-3 precursor
- integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)
- platelet glycoprotein IIIa
- platelet GPIIIa
- platelet membrane glycoprotein IIIa
- vitronectin receptor beta chain

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