\( \alpha_{IIb} \beta_3 \): The Key to Platelet Aggregation (and Clotting)

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The Story of \( \alpha_{IIb} \beta_3 \)

Blood coagulation, or the clotting of blood, is a vital process in the body wherein a damaged area of a blood vessel is blocked by platelets and fibrin to stop bleeding until it can be repaired. This process involves proteins known as integrins, a kind of integral membrane protein, which mediate cell-cell and cell-surface interactions. Integrin \( \alpha_{IIb} \beta_3 \), comprised of two glycoprotein subunits and acting as a transmembrane protein on the surface of platelets, and plays a crucial role in the clotting process by acting as a receptor for proteins that mediate the interaction of one platelet to another.

When a blood vessel is damaged, proteins under the endothelial layer of the blood vessel are exposed at the site of injury. Other receptors cause platelets to bind to the site of damage. This initial binding causes the platelets to become activated, which causes the release of many substances supportive of the clotting process, and also results in the activation of \( \alpha_{IIb} \beta_3 \). It is vital that the activation of \( \alpha_{IIb} \beta_3 \) is controlled, as an overly large amount of activated \( \alpha_{IIb} \beta_3 \) would cause excessive clotting. During activation, the structure of \( \alpha_{IIb} \beta_3 \) changes dramatically, converting from a bent, inactive conformation, into a comparatively ‘straight’ protein. These changes occur in the integrin because a salt bridge between the intracellular domains of \( \alpha \) and \( \beta \) is broken. As a result of this conformational change, amino acids are exposed which form the binding site for several plasma proteins which adhere to the damaged blood vessel, including fibrinogen, von Willebrand Factor, fibronectin, and vitronectin. The binding of fibrinogen cross-links the platelets and results in platelet aggregation at the site of damage. Despite intensive study, the changes leading to the activation of \( \alpha_{IIb} \beta_3 \) functions are still being clarified. However, because blood clotting plays a role in cardiovascular diseases, scientists are working hard to fully understand the structure and function of \( \alpha_{IIb} \beta_3 \) and its role in platelet aggregation.

Why Does Clotting Matter?

Blood clotting is a delicate balance that requires the rapid ability of platelets to activate and stem blood flow. If there is too much activation of platelets, there will be too much clotting, forming a clot in the blood vessel. This could lead to a variety of dangerous health conditions, including heart attack and stroke. Too little clotting can cause severe bleeding (exsanguination). An improper amount of clotting may be due to an insufficient amount of activated \( \alpha_{IIb} \beta_3 \).

Integrins are integral membrane proteins on the surface of cells and act as receptors, receiving and sending signals through the cells through inside-out or outside-in communication. In the case of \( \alpha_{IIb} \beta_3 \), this signal, activated when a platelet comes into contact with damaged blood vessel, triggers the binding of fibrinogen (or the clotted form called fibrin), helping to aggregate platelets into clots.

Here, one \( \alpha_{IIb} \beta_3 \) integrin on the surface of a platelet interacts with an \( \alpha_{IIb} \beta_3 \) integrin on another through binding of bivalent fibrinogen. This process mediates the binding of one platelet to another, known as platelet aggregation.

Related Medical Conditions

In Glanzmann’s thrombasthenia, \( \alpha_{IIb} \beta_3 \) is missing or abnormal due to genetically defective proteins. This abnormality leads to improper clotting and a bleeding disorder.

The \( \alpha_{IIb} \beta_3 \) Activation Process

Blood vessel damage signals \( \alpha_{IIb} \beta_3 \) when the platelet is exposed to the sub-endothelial tissues of the damaged blood vessel.

This process leads \( \alpha_{IIb} \beta_3 \) to activate, and it in turn begins to facilitate the binding of fibrin. In this active form, which we modeled, the legs are separated and the extracellular domain, formerly bent, is upright. Fibrinogen binds at the blue top, where the \( \alpha \) and \( \beta \) subunits meet.