Tyrosine Phosphorylation of the Integrin B3 Subunit Regulates B3 Cleavage by Calpain

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Technology description

An anti-peptide antibody that specifically recognizes phosphorylated 759 tyrosine on β3 cytoplasmic domain and does not recognize non-phosphorylated tyrosine on β3 cytoplasmic domain. This is useful for studying "outside-in" cellular signaling.

Cell signaling is part of a complex system of communication that governs basic cellular activities and coordinates cell actions. The ability of cells to perceive and correctly respond to their microenvironment is the basis of development, tissue repair, and immunity as well as normal tissue homeostasis.

Errors in cellular information processing are responsible for diseases such as cancer, autoimmunity, and diabetes. By understanding cell signaling, diseases can be treated effectively and, theoretically, artificial tissues could be built.

Tools for investigating the "outside-in" signaling, which plays a vital role in cell adhesion, cell activation, cell spreading, and retraction are not widely available.

The present invention is a medical invention related specifically to "outside-in" cell signaling research. The invention in particular is related to a method of investigation of integrin signaling leading to cell adhesion, cell activation, spreading, and retraction.

The present invention provides an anti-peptide antibody that can specifically recognize phosphorylated tyrosine residues on β3 cytoplasmic domain as opposed to nonphosphorylated tyrosine residues, and can be useful for understanding specific cell signaling mechanisms more clearly.

The inventors have found that tyrosine phosphorylation in the β3 cytoplasmic domain of IntegrinIIbβ3 inhibits β3 cleavage by calpain, and thus phosphorylation positively regulates "outside-in" signaling.

In order to detect β3 tyrosine phosphorylation both in vitro and in platelets, the present inventors have developed an anti-peptide antibody that specifically recognizes phosphorylated 759 tyrosine on β3 cytoplasmic domain and does not recognize non-phosphorylated tyrosine on β3 cytoplasmic domain.

It was also shown that thrombin, which is activated in the coagulation cascade, induces phosphorylation on the tyrosine 759 (Tyr759) residue of β3, and protects β3 from calpain cleavage.

This antibody specifically recognizes phosphorylated 759 Tyrosine on B3 cytoplasmic domain and do [sic] not recognize non-phosphorylated tyrosine or B3 cytoplasmic domain.

Advantages

Cell signaling

Elucidation of integrin signaling leading to cell adhesion, cell activation, spreading, and retraction by the method of the present invention will lead to development of more efficient treatment of various diseases which are related to defective cell signaling.

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