



ANTIBODY CHARACTERISTICS

Name: Integrin Beta3 Antibody 762

Target Species: Human

Status: Available

Description: Cleavage by calpain differentially regulates the function of b3 integrins which are involved in cell adhesion. This antibody specifically binds one of the four known cleavage sites for detection of calpain-downregulated integrins in platelets.

<u>Type</u>	<u>Location</u>	<u>Purification</u>	<u>Tested Applications</u>		<u>Available</u>
<input type="checkbox"/> Monoclonal	<input type="checkbox"/> Nuclear	<input checked="" type="checkbox"/> None	<input checked="" type="checkbox"/> Histology	<input type="checkbox"/> Flow	<input checked="" type="checkbox"/> Crude Ab
<input checked="" type="checkbox"/> Polyclonal	<input checked="" type="checkbox"/> Cytoplasm	<input type="checkbox"/> Am. Sulfate	<input type="checkbox"/> Cytology	<input type="checkbox"/> ELISA	<input type="checkbox"/> Purified Ab
<input type="checkbox"/> Engineered	<input type="checkbox"/> Membrane	<input type="checkbox"/> Chromato.	<input type="checkbox"/> Precipitation	<input type="checkbox"/> Therapy	<input type="checkbox"/> Immunogen
	<input type="checkbox"/> Secreted	<input type="checkbox"/> Affinity	<input checked="" type="checkbox"/> Blotting	<input type="checkbox"/> Other	<input type="checkbox"/> Hybridoma
		<input type="checkbox"/> Other			<input type="checkbox"/> Controls



Antibodies Specific for the $\beta 3$ -subunit of Integrin $\alpha \text{IIb}\beta 3$

Technology Reference

CW-004

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Fields

Pharmacology
Coagulation

Key Words

Integrin
Cell adhesion
Platelet adhesion
Blood clotting
Calpain
Thrombosis
Hemostasis

Stage of Development

Animal model available

Patent Status

Provisional Application
Filed

Status

Seeking Licensing Partner

Applications

- Coagulation Research
- Diagnostic Testing

This Invention

This invention consists of five monoclonal antibodies that bind to specific sites that are exposed by the calpain-mediated cleavage of the $\beta 3$ subunit of integrin $\alpha \text{IIb}\beta 3$. Binding of the antibodies against sites 762 and 759 correlate with down regulation of the “inside-out” signaling pathway that controls platelet adhesion while antibody binding to the 754, 747 and/or 741 sites correlates with down regulation of both the inside-out and “outside-in” pathways. The outside-in pathway controls cell spreading and the stabilization of platelet adhesion.

Applications

These antibodies permit the determination of the state of regulation of integrin $\alpha \text{IIb}\beta 3$ in platelets relative to cell adhesion, clot formation and clot stabilization. Increased binding of the Mab 759 and 762 antibodies correlates with decreased cell adhesion while increased binding of Mab 741, 747 and 754 correlates with decreased cell adhesion, clot formation and clot stabilization.

Prior Art and Background

Integrin $\alpha \text{IIb}\beta 3$ on circulating platelets is normally in a resting state with low ligand affinity. Activation of platelets by agonists such as thrombin induces “inside-out” signals that activates ligand binding function of Integrin $\alpha \text{IIb}\beta 3$. The binding of ligands such as fibrinogen in turn triggers an “outside-in” signaling pathway that leads to cell spreading, stabilization of cell adhesion and a secondary wave of platelet aggregation. Data suggests that these signaling processes are at least partially regulated by the calpain-mediated cleavage of integrin $\alpha \text{IIb}\beta 3$ at specific sites on the $\beta 3$ subunit. Cleavage at site Y759 has no significant effect on inside-out signaling, but significantly reduces outside-in signaling. Cleavage at site F754 or at sites N-terminal to F754 down regulates both signaling pathways. It is speculated that calpain-mediated cleavage of integrin $\alpha \text{IIb}\beta 3$ both suppresses partially activated resting platelets and terminates platelet aggregation after clot formation.

Benefits

.These antibodies provide a means of determining and monitoring the regulatory and activation status of platelets during the clotting process.



Antibodies Specific for the **β 3-subunit of Integrin α IIb β 3**

References

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2. Du, X., Saido, TC., Tsubuki, S., Indig, FE., Williams, MJ., Ginsberg, MH. Calpain cleavage of the cytoplasmic domain of the integrin beta 3 subunit. *J. Biol. Chem.* 1995; 270:26146-51.
3. Gu, M., Xi, X., Englund, GD., Berndt, MC., Du, X. Analysis of the roles of 14-3-3 in the platelet glycoprotein Ib-IX-mediated activation of integrin alpha(Iib)beta(3) using a reconstituted mammalian cell expression model. *J. Cell Biol.* 1999; 147:1085-96.

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Research Focus

Thrombosis, hemostasis and vascular biology with a focus on the molecular mechanisms and molecular pharmacology of platelet and endothelial cell function.

- Signaling and regulatory mechanisms of the platelet adhesion receptor glycoprotein Ib-IX complex.
- Protein kinase signaling cascades leading to platelet activation, particularly the activation of platelet integrin α IIb β 3.
- Regulatory mechanisms of integrins in platelets and endothelial cells.

Awards

- American Heart Association Established Investigator Award
- NIH FIRST Award