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Calcium Integrin Binding Protein Associates with Integrins $\alpha_V\beta_3$ and $\alpha_{IIb}\beta_3$ Independent of β_3 Activation Motifs

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ABSTRACT

The Calcium Integrin Binding protein (CIB) has been identified as interacting specifically with the cytoplasmic tail of the integrin α_{IIb} domain to induce receptor activation and integrin $\alpha_{IIb}\beta_3$ mediated cell adhesion to extracellular proteins. In K562 cells stably expressing mutated integrin $\alpha_V\beta_3$ or chimeric $\alpha_V\beta_3$ carrying α_{IIb} cytoplasmic tail, we report that the interaction of CIB with β_3 integrins is not $\alpha_{IIb}\beta_3$ specific but binds α_{IIb} as well as α_V cytoplasmic tail domains. A double mutation of two proline residues to alanine residues in the α_{IIb} cytoplasmic domain, previously shown to disturb its conformation, inhibits chimeric $\alpha_V/\alpha_{IIb}\beta_3$-CIB interaction. This demonstrates that α_{IIb} cytoplasmic domain loop-like conformation is required for interaction with CIB. Moreover, mutations of $\beta3$ cytoplasmic domain residues Tyr-747 and/or Tyr-759 to phenylalanine residues (Y747F, Y759F, and Y747,759F) as well as residues Ser-752 to proline or alanine (S752P and S752A), do not affect the $\alpha_{IIb}\beta_3$ or $\alpha_V\beta_3$ interaction with CIB. Since tyrosine residues Tyr-747 and/or Tyr-759 are the sites of tyrosine phosphorylation of β_3 subunit, these results suggest that the β_3 integrin-CIB interaction occurs through aβ_3-phosphorylation independent mechanism. Likewise, ablation of conformation-dependent affinity change in β_3 Ser752Pro mutation had no affect on CIB-β_3 interaction. In summary, our results demonstrate that the α_{IIb}-subunit integrin and CIB interaction is non-exclusive and requires the loop-like α_{IIb}-cytoplasmic domain conformation. An interaction of CIB with α_V-containing integrins provides an additional role for this molecule in keeping with its expression outside of platelets.

KEYWORDS

Leukocyte; Integrin; Cytoskeleton; Hematopoietic; Activation; Signaling

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References

[1] U. P. Naik, P. M. Patel and L. V. Parise, "Identification of a Novel Calcium-Binding Protein That Interacts with the Integrin AlphaIIb Cytoplasmic Domain," The Journal of Biological Chemistry, Vol. 272, No. 8, 1997, pp. 4651- 4654.

[2] L. Vallar, C. Melchior, S. Plancon, H. Drobecq, G. Lippens, V. Regnault and N. Kieffer, "Divalent Cations Differentially Regulate Integrin AlphaIIb Cytoplasmic Tail Binding to beta3 and to Calciumand Integrin-Binding Protein," The Journal of Biological Chemistry, Vol. 274, No. 24, 1999, pp. 17257-17266.

[3] W. T. Barry, C. Boudignon-Proudhon, D. D. Shock, A. McFadden, J. M. Weiss, J. Sondek and L. V. Parise, "Molecular Basis of CIB Binding to the Integrin Alpha IIb Cytoplasmic Domain," The Journal of Biological Chemistry, Vol. 277, No. 32, 2002, pp. 28877-28883.

[4] P. M. Hwang and H. J. Vogel, "Structures of the Platelet Calcium- and Integrin-Binding Protein and the AlphaIIb-Integrin Cytoplasmic Domain Suggest a Mechanism for Calcium-Regulated Recognition; Homology Modelling and NMR Studies," Journal of Molecular Recognition, Vol. 13, No. 2, 2000, pp. 83-92. doi:10.1002/(SICI)1099-1352(200003/04)13:2<83::AID-JMR491>3.0.CO;2-A

[5] S. Tsuboi, "Calcium Integrin-Binding Protein Activates Platelet Integrin Alpha IIbbeta 3," The

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Journal of Biological Chemistry, Vol. 277, No. 3, 2002, pp. 1919-1923.

[6] U. P. Naik and M. U. Naik, "Association of CIB with GPIIb/IIIa during Outside-In Signaling Is Required for Platelet Spreading on Fibrinogen," Blood, Vol. 102, 4, pp. 1355-1362.

[7] M. U. Naik and U. P. Naik, "Calcium-and IntegrinBinding Protein Regulates Focal Adhesion Kinase Activity during Platelet Spreading on Immobilized Fibrinogen," Blood, Vol. 102, No. 10, 2003, pp. 3629-3636.

[8] L. Haataja, V. Kaartinen, J. Groffen and N. Heisterkamp, "The Small GTPase Rac3 Interacts with the integrinBinding Protein CIB and Promotes Integrin Alpha(IIb) Beta(3)-Mediated Adhesion and Spreading," The Journal of Biological Chemistry, Vol. 277, No. 10, 2002, pp. 8321-8328.

[9] S. Ma, M. A. Liu, Y. L. Yuan and R. L. Erikson, "The Serum-Inducible Protein Kinase Snk Is a G1 Phase Polo-Like Kinase That Is Inhibited by the Calcium- and Integrin-Binding Protein CIB," Molecular Cancer Research, Vol. 1, No. 5, 2003, pp. 376-384.

[10] C. Whitehouse, J. Chambers, K. Howe, M. Cobourne, P. Sharpe and E. Solomon, "NBR1 Interacts with Fasciculation and Elongation Protein Zeta-1 (FEZ1) and Calcium and Integrin Binding Protein (CIB) and Shows Developmentally Restricted Expression in the Neural Tube," European Journal of Biochemistry, Vol. 269, No. 2, 2002, pp. 538-545. doi:10.1046/j.0014-2956.2001.02681.x

[11] O.Vinogradova, A. Velyvis, A. Velyviene, B. Hu, T. Haas, E. Plow and J. Qin, "A Structural Mechanism of Integrin Alpha(IIb)Beta(3) 'Inside-Out' Activation as Regulated by Its Cytoplasmic Face," Cell, Vol. 110, No. 5, 2002, pp. 587-597.

[12] A. M. Weljie, P. M. Hwang and H. J. Vogel, "Solution Structures of the Cytoplasmic Tail Complex from Platelet Integrin Alpha IIb- and Beta 3-Subunits," Proceedings of the National Academy of Sciences, Vol. 99, No. 9, 2002, pp. 5878-5883.

[13] T M. Leisner, J. D. Wencel-Drake, W. Wang and S. C. Lam, "Bidirectional Transmembrane Modulation of Integrin AlphaIIbBeta3 conformations," The Journal of Biological Chemistry, Vol. 274, No. 18, 1999, pp. 12945-12949.

[14] S. D. Blystone, M. P. Williams, S. E. Slater and E. J. Brown, "Requirement of Integrin Beta3 Tyrosine 747 for Beta3 Tyrosine Phosphorylation and Regulation of Alphavbeta3 Avidity," The Journal of Biological Chemistry, Vol. 272, No. 45, 1999, pp. 28757-28761.

[15] S. D. Blystone, "Kinetic Regulation of Beta 3 Integrin Tyrosine Phosphorylation," The Journal of Biological Chemistry, Vol. 277, No. 49, 2002, pp. 46886-46890.

[16] T. E. O'Toole, J. Ylanne and B. M. Culley, "Regulation of Integrin Affinity States through an NPXY Motif in the Beta Subunit Cytoplasmic Domain," The Journal of Biological Chemistry, Vol. 270, No. 15, 1995, pp. 8553-8558. doi:10.1074/jbc.270.15.8553

[17] P. D. Tahiliani, L. Singh, K. L. Auer and S. E. LaFlamme, "The Role of conserved Amino Acid Motifs within the Integrin Beta3 Cytoplasmic Domain in Triggering Focal Adhesion Kinase Phosphorylation," The Journal of Biological Chemistry, Vol. 272, No. 12, 1997, 7892-7898. doi:10.1074/jbc.272.12.7892

[18] A. A. De Melker, D. Kramer, I. Kuikman and A. Sonnenberg, "The two Phenylalanines in the GFFKR Motif of the Integrin Alpha6A Subunit Are Essential for Heterodimerization," Biochemical Journal, Vol. 328, 1997, pp. 529-537.

[19] R. Pardi, G. Bossi, L. Inverardi, E. Rovida and J. R. Bender, "Conserved Regions in the Cytoplasmic Domains of the Leukocyte Integrin Alpha L Beta 2 Are Involved in Endoplasmic Reticulum Retention, Dimerization, and Cytoskeletal Association," The Journal of Immunology, Vol. 155, No. 3, 1995, pp. 1252-1263.

[20] E. Loh, W. Qi, G. Vilaire and J. S. Bennett, "Effect of Cytoplasmic Domain Mutations on the Agonist-Stimulated Ligand Binding Activity of the Platelet Integrin AlphaIIbBeta3," The Journal of Biological Chemistry, Vol. 271, No. 47, 1996, pp. 30233-30241.

[21] T. E. O'Toole, Y. Katagiri, R. J. Faull, K. Peter, R. Tamura, V. Quaranta, J. C. Loftus, S. J. Shattil and M. H. Ginsberg, "Integrin Cytoplasmic Domains Mediate Inside-Out Signal Transduction," The Journal of Cell Biology, Vol. 124, No. 6, 1994, pp. 1047-1059.

[22] P. E. Hughes, T. E. O'Toole, J. Ylanne, S. J. Shattil and M. H. Ginsberg, "The Conserved Membrane-Proximal Region of an Integrin Cytoplasmic Domain Specifies Ligand Binding Affinity," The Journal of Biological Chemistry, Vol. 270, No. 21, 1995, pp. 12411-1247.

[23] T. E. O ' Toole, J. Mandelman, J. Foryth, S. J. Shattil and M. H. Ginsberg, " Modulation of the Affinity of Integrin Alpha IIb Beta 3 (GPIIb-IIIa) by the Cytoplasmic Domain of Alpha IIb, " Science, Vol. 254, No. 5033, 1991, pp. 845-847. doi:10.1126/science.1948065

[24] D. F. Kucik, T. E. O ' Toole, A. Zheleznyak, D. K. Busettini and E. J. Brown, " Activation-Enhanced Alpha(IIb) Beta(3)-Integrin-Cytoskeleton Interactions outside of Focal Contacts Require the Alpha-Subunit, " Molecular Biology of the Cell, Vol. 12, No. 5, 2001, pp. 1509-1518.

[25] T. A. Haas and E. F. Plow, " The Cytoplasmic Domain of Alphaiib Beta3. A Ternary Complex of the Integrin Alpha and Beta Subunits and a Divalent Cation, " The Journal of Biological Chemistry, Vol. 271, No. 11, 1996, pp. 6017-6026.

[26] O. Vinogradova, T. Haas, E. F. Plow and J. Qin, " A Structural Basis for Integrin Activation by the Cytoplasmic Tail of the Alpha IIb-Subunit, " Proceedings of the National Academy of Sciences, Vol. 4, 2000, pp. 1450-1455. doi:10.1073/pnas.040548197

[27] C. Spillmann, D. Osorio and R. A. Waugh, " Integrin Activation by Divalent Ions Affects Neutrophil Homotypic Adhesion, " Biomedical Engineering, Vol. 30, No. 8, 2002, pp. 1002-1011.

[28] A. P. Yamniuk, L. T. Nguyen, T. T. Hoang and H. J. Vogel, " Metal Ion Binding Properties and Conformational States of Calcium- and Integrin-Binding Protein, " Biochemistry, Vol. 43, No. 9, 2004, pp. 2558-2568.