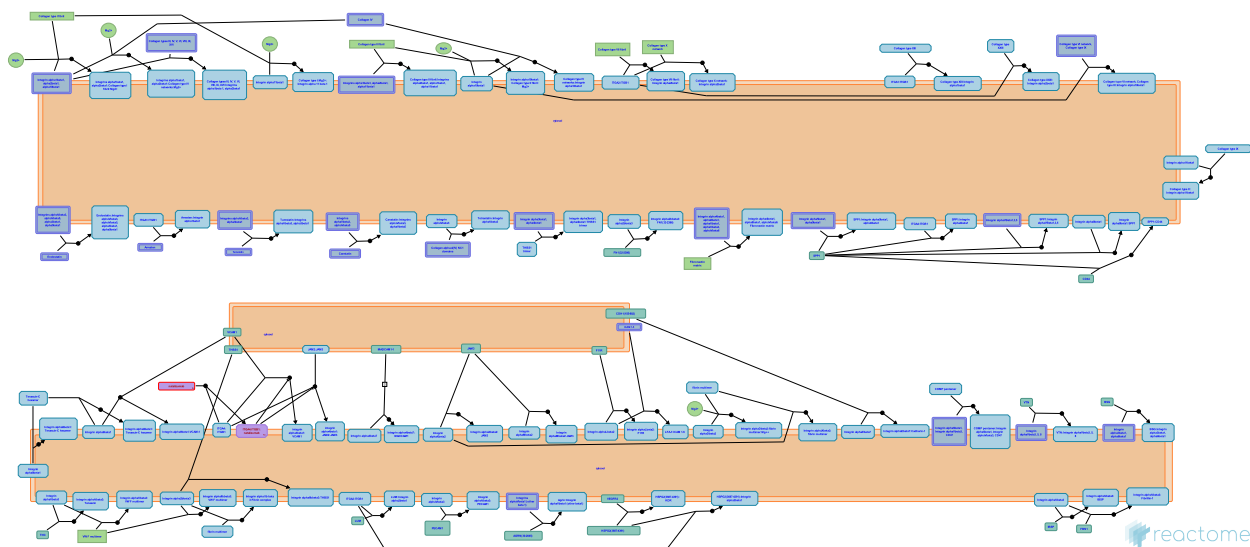


# Integrin cell surface interactions



Barrow, AD., Garapati, P V., Geiger, B., Horwitz, AR., Humphries, MJ., Hynes, R., Jassal, B., Jupe, S., Ouwehand, WH., Ricard-Blum, S., Shoichet, BK., Trowsdale, J., Yamada, KM., Zwaginga, JJ., de Bono, B.

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/page/about-us).

02/12/2024

## Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

## Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)

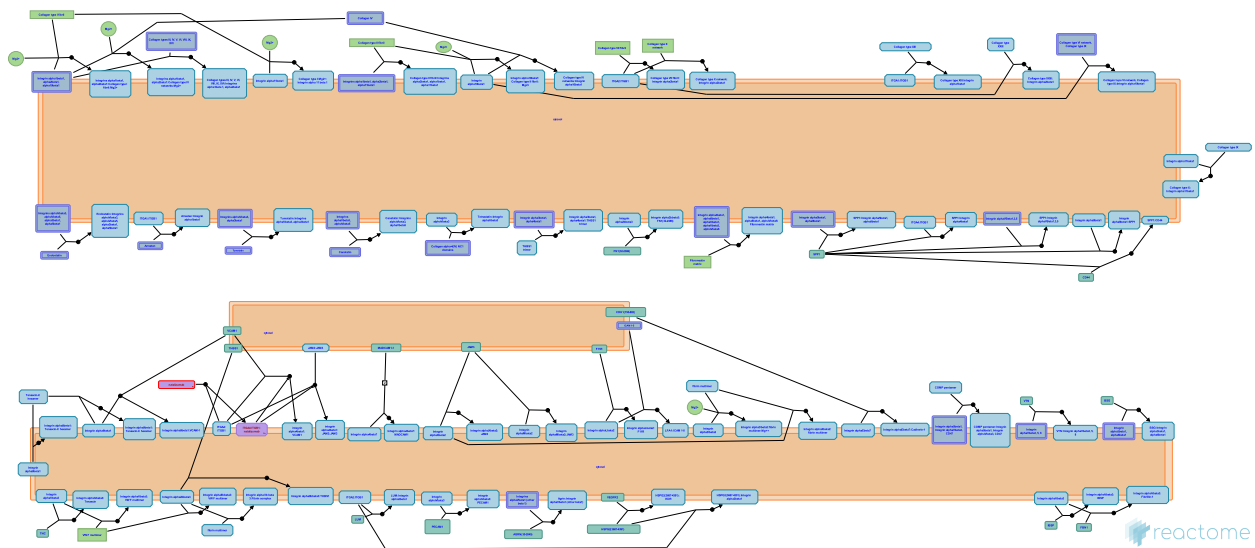
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 90

This document contains 1 pathway and 55 reactions ([see Table of Contents](#))

# Integrin cell surface interactions ↗

Stable identifier: R-HSA-216083



The extracellular matrix (ECM) is a network of macro-molecules that underlies all epithelia and endothelia and that surrounds all connective tissue cells. This matrix provides the mechanical strength and also influences the behavior and differentiation state of cells in contact with it. The ECM are diverse in composition, but they generally comprise a mixture of fibrillar proteins, polysaccharides synthesized, secreted and organized by neighboring cells. Collagens, fibronectin, and laminins are the principal components involved in cell matrix interactions; other components, such as vitronectin, thrombospondin, and osteopontin, although less abundant, are also important adhesive molecules. Integrins are the receptors that mediate cell adhesion to ECM. Integrins consists of one alpha and one beta subunit forming a noncovalently bound heterodimer. 18 alpha and 8 beta subunits have been identified in humans that combine to form 24 different receptors.

The integrin dimers can be broadly divided into three families consisting of the beta1, beta2/beta7, and beta3/alphaV integrins. beta1 associates with 12 alpha-subunits and can be further divided into RGD-, collagen-, or laminin binding and the related alpha4/alpha9 integrins that recognise both matrix and vascular ligands. beta2/beta7 integrins are restricted to leukocytes and mediate cell-cell rather than cell-matrix interactions, although some recognize fibrinogen. The beta3/alphaV family members are all RGD receptors and comprise aIIBb3, an important receptor on platelets, and the remaining b-subunits, which all associate with alphaV. It is the collagen receptors and leukocyte-specific integrins that contain alpha A-domains.

## Literature references

Jones, PL., Boudreau, NJ. (1999). Extracellular matrix and integrin signalling: the shape of things to come. *Biochem. J.*, 339, 481-8. ↗

Watson, LE., Lal, H., Singh, H., Reneau, JC., Verma, SK., Golden, HB. et al. (2009). Integrins and proximal signaling mechanisms in cardiovascular disease. *Front. Biosci.*, 14, 2307-34. ↗

Faull, RJ., Ginsberg, MH. (1996). Inside-out signaling through integrins. *J Am Soc Nephrol*, 7, 1091-7. ↗

Goodman, SL., Arnaout, MA., Xiong, JP. (2002). Coming to grips with integrin binding to ligands. *Curr Opin Cell Biol*, 14, 641-51. ↗

White, DJ., Johnson, MS., Heino, J., Puranen, S. (2004). The collagen receptor subfamily of the integrins. *Int J Bio-chem Cell Biol*, 36, 1405-10. ↗

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.
2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

## Collagen types III, IV, V, VI, VIII, IX, XVI bind integrins alpha1beta1 and alpha2beta1

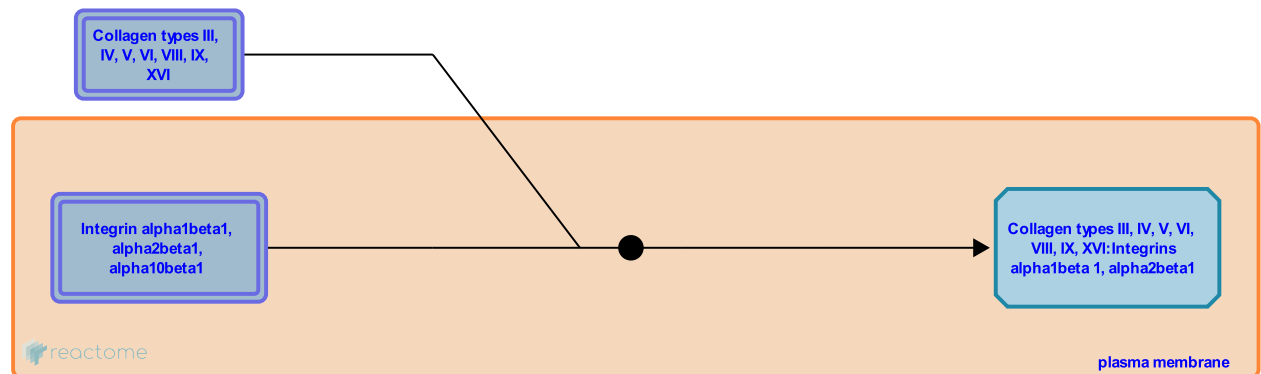


**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-2327695

**Type:** binding

**Compartments:** plasma membrane, extracellular region



The widely-expressed collagen receptors integrin alpha2beta1 and alpha1beta1 both bind collagen types I-IV (Tulla et al. 2001). Integrin alpha1beta1 binds to collagen type IV and VI with higher affinity than to types I-III, whereas alpha2beta1 has a higher affinity for collagen types I-III than for type IV (Tulla et al. 2001). Binding to collagen type I occurs at a site corresponding to residues 502-516 of the collagen alpha-1(I) chain (Knight et al. 1998, 2000, Xu et al. 2000).

Integrin alpha2beta1 also binds collagen types VIII (Saelman et al. 1992), IX (Käpylä et al. 2004), XI (Tuckwell et al. 1995), the noncollagenous domain 1 (NC1) of collagen types VII and X (Chen et al. 1999), and collagen type XVI, though this is bound with higher affinity by integrin alpha1beta1 (Eble et al. 2006). Both integrins interact with collagen XVI via the A-domain of their alpha-subunits. A tryptic fragment of collagen XVI comprising collagenous domains 1-3 is bound by integrin alpha1beta1. Electron microscopy of this complex or integrin alpha1beta1 with full-length collagen XVI revealed two unique integrin alpha1beta1 binding sites (GLQGER and GIKGER) within the N-terminal half of the COL2 domain of collagen XVI (Grässel & Bauer 2013).

Integrin alpha1beta1 also binds collagen types IX (Käpylä et al. 2004), XVI (Eble et al. 2006), VIII though less strongly than alpha2beta1 (Saelman et al. 1992), XIII (Nykqvist et al. 2000) and arresten, the NC1 of alpha-1 type IV collagen (Colorado PC et al. 2000; Nyberg et al. 2008).

Integrin alpha10beta1 is able to bind collagen types I-VI, with a stronger binding affinity for types IV and VI, similar to the preferences of integrin alpha1beta1 (Tulla et al. 2001).

Integrin alpha11beta1 mediates cell adhesion to collagen types I and IV with a preference for I (Tiger et al. 2001).

Integrins alphaVbeta3 (Sudhakar et al. 2003) and alpha3beta1 (Borza et al. 2006) can bind tumstatin, the cleaved NC1 of alpha-3 type IV collagen. Integrins alphaVbeta3 and alphavbeta5 can bind camstatin, the cleaved NC1 of alpha-2 type IV collagen (Magnon et al. 2005).

### Literature references

- Nissinen, L., Jääliñoja, J., Heino, J., Vehviläinen, P., Farndale, RW., Viitasalo, T. et al. (2004). The fibril-associated collagen IX provides a novel mechanism for cell adhesion to cartilaginous matrix. *J. Biol. Chem.*, 279, 51677-87. [↗](#)
- Niland, S., Kassner, A., Grässel, S., Mörgelin, M., Grifka, J., Eble, JA. (2006). Collagen XVI harbors an integrin alpha1beta1 recognition site in its C-terminal domains. *J Biol Chem*, 281, 25745-56. [↗](#)
- Nieuwenhuis, HK., Williams, S., Gralnick, HR., Saelman, EU., McKeown, L., Sage, EH. et al. (1994). Platelet adhesion to collagen types I through VIII under conditions of stasis and flow is mediated by GPIa/IIa (alpha 2 beta 1-integrin). *Blood*, 83, 1244-50. [↗](#)

Kühn, K., Golbik, R., Eble, J., Kern, A. (1993). Interaction of type IV collagen with the isolated integrins alpha 1 beta 1 and alpha 2 beta 1. *Eur. J. Biochem.*, 215, 151-9. [↗](#)

Nissinen, L., Nykvist, P., Johnson, MS., Impola, U., Viitasalo, T., Tulla, M. et al. (2001). Selective binding of collagen subtypes by integrin alpha 1I, alpha 2I, and alpha 10I domains. *J. Biol. Chem.*, 276, 48206-12. [↗](#)

## Editions

2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

**Collagen type I binds integrin alpha1beta1, alpha2beta1, alpha10beta1** ↗

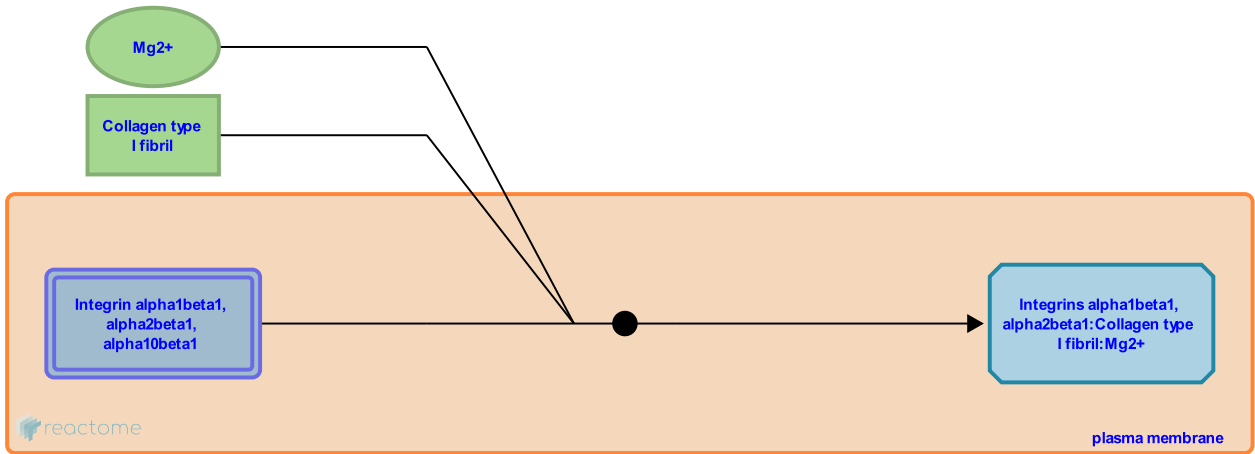
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-114563

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Inferred from:** [Collagen type I binds integrin alpha1beta1, alpha2beta1, alpha10beta1 \(Homo sapiens\)](#)



Integrin alpha1beta1 binds to collagen type IV and VI with higher affinity than to types I-III, whereas alpha2beta1 has a higher affinity for collagen types I-III than for type IV. Integrin alpha10beta1 binds collagen types I, IV, and VI with similar affinities (Tulla et al. 2001). Integrin alpha11beta1 binds preferentially to the fibril-forming collagen types I and II, binding to type III is weaker and collagens IV and VI are poor ligands (Zhang et al. 2003).

Binding to collagen type I occurs at sites corresponding to the six-residue sequence G(F/L)OGER (Knight et al. 1998, 2000, Xu et al. 2000).

Integrin alpha2beta1 is the major platelet collagen receptor (Kunicki et al. 1988). It requires Mg<sup>2+</sup> to interact with collagen and may require initiation mediated by the activation of Integrin alphaIIbBeta3 (van de Walle 2007).

**Editions**

2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.
2013-08-13	Revised	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

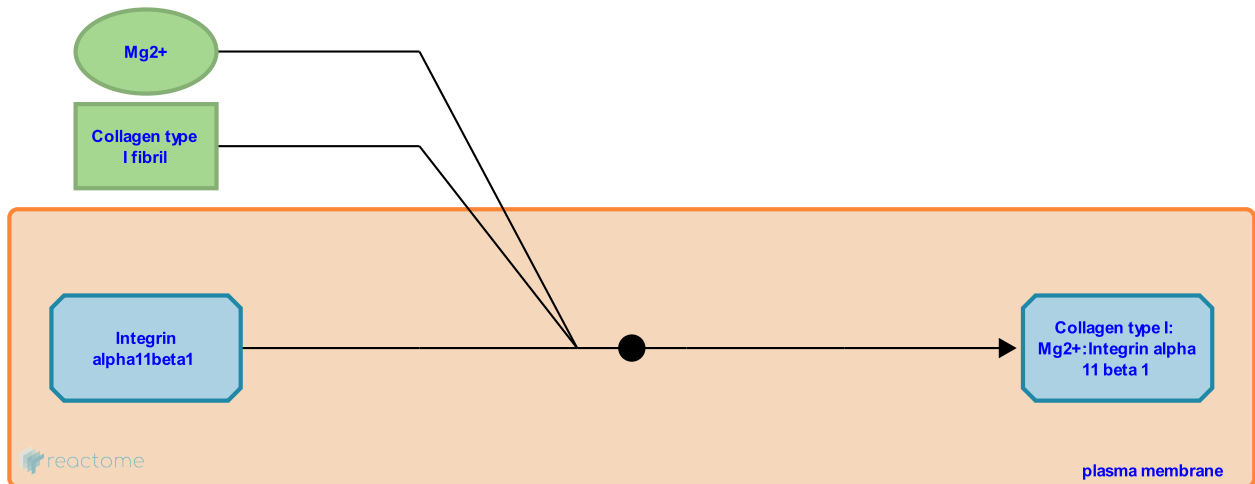
## Collagen type I binds integrin alpha11beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216045

**Type:** binding

**Compartments:** plasma membrane, extracellular region



The integrin alpha11beta1 along with alpha1beta1, alpha2beta1 and alpha10beta1 are referred to as a collagen receptor subgroup of the integrin family. Integrin alpha11beta1 binds preferentially to the fibril-forming collagen types I and II, binding to type III is weaker and collagens IV and VI are poor ligands (Zhang et al. 2003).

### Literature references

Fougerousse, F., Grundstrom, G., Gullberg, D., Tiger, CF., Velling, T. (2001). alpha11beta1 integrin is a receptor for interstitial collagens involved in cell migration and collagen reorganization on mesenchymal nonmuscle cells. *Dev Biol*, 237, 116-29. ↗

Knight, CG., Puranen, JS., Johnson, MS., Heino, J., Farndale, RW., Gullberg, D. et al. (2003). alpha 11beta 1 integrin recognizes the GFOGER sequence in interstitial collagens. *J Biol Chem*, 278, 7270-7. ↗

### Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

## Collagen type II binds integrin alpha2beta1, alpha1beta1, alpha11beta1 ↗

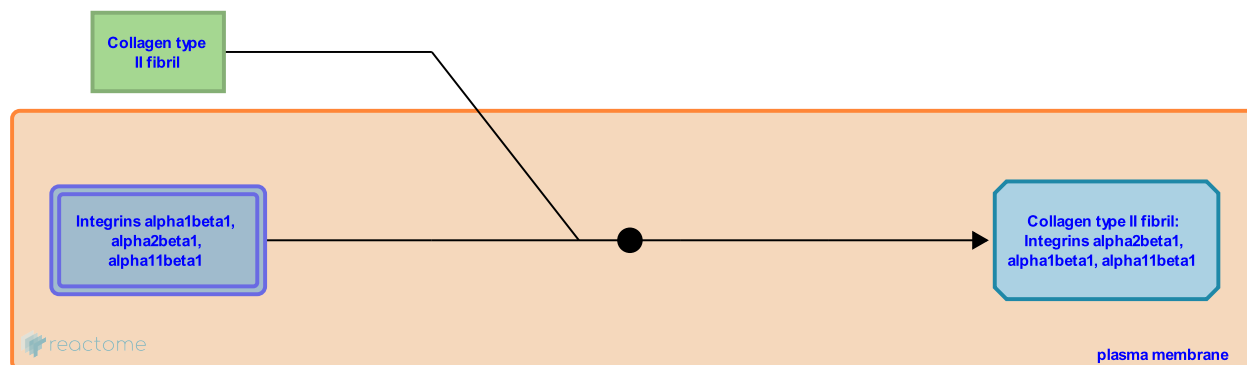
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4084910

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Inferred from:** [Collagen type II binds integrin alpha2beta1, alpha1beta1, alpha11beta1 \(Homo sapiens\)](#)



The widely-expressed collagen receptors integrin alpha2beta1 and alpha1beta1 both bind collagen types I-IV (Tulla et al. 2001). Integrin alpha1beta1 binds to collagen type IV and VI with higher affinity than to types I-III, whereas alpha2beta1 has a higher affinity for collagen types I-III than for type IV (Tulla et al. 2001).

### Editions

2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.



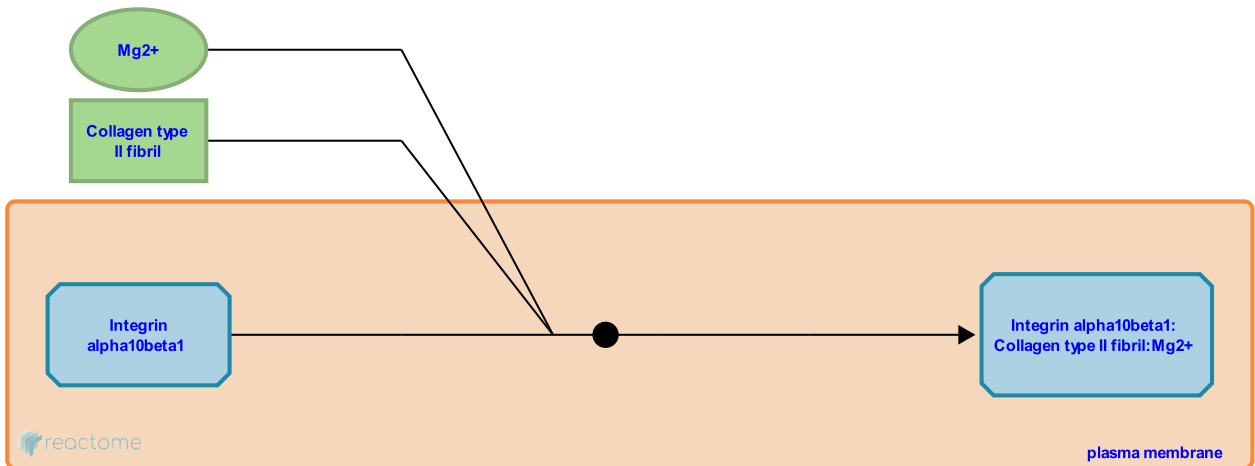
# Collagen type II binds integrin alpha10beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216043

**Type:** binding

**Compartments:** plasma membrane, extracellular region



The integrin alpha10beta1 is a collagen type II-binding integrin on chondrocytes. This integrin is of great importance during chondrogenesis. alpha10 binds the collagen-II with its I domain displaying similar binding properties as alpha1 I domain.

## Literature references

Bengtsson, T., Lundgren-Akerlund, E., Aszodi, A., Fässler, R., Hunziker, EB., Nicolae, C. (2005). Loss of alpha10beta1 integrin expression leads to moderate dysfunction of growth plate chondrocytes. *J Cell Sci*, 118, 929-36. ↗

## Editions

2008-03-11	Edited	Garapati, P V.
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**Collagen type IV networks bind integrins alpha1beta1, alpha2beta1 ↗**

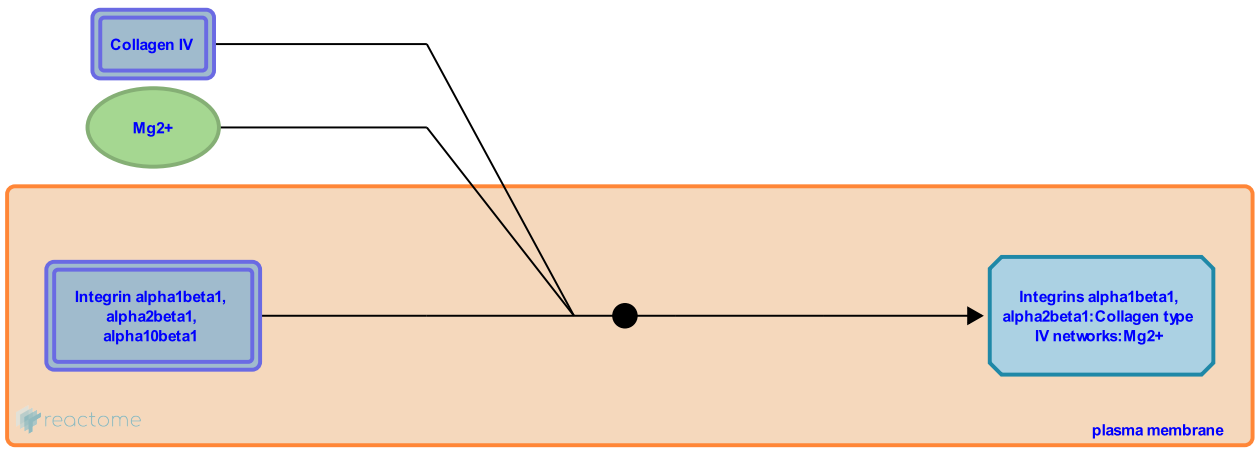
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216040

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Inferred from:** [Collagen type IV binds integrin alpha2beta1, alpha1beta1 \(Homo sapiens\)](#)



The collagen receptors integrin alpha2beta1 and alpha1beta1 bind collagen types I-IV (Tulla et al. 2001). Integrin alpha1beta1 binds to collagen type IV and VI with higher affinity than to types I-III, whereas alpha2beta1 has a higher affinity for collagen types I-III than for type IV (Tulla et al. 2001).

**Editions**

2008-03-11	Edited	Garapati, P V.
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2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.
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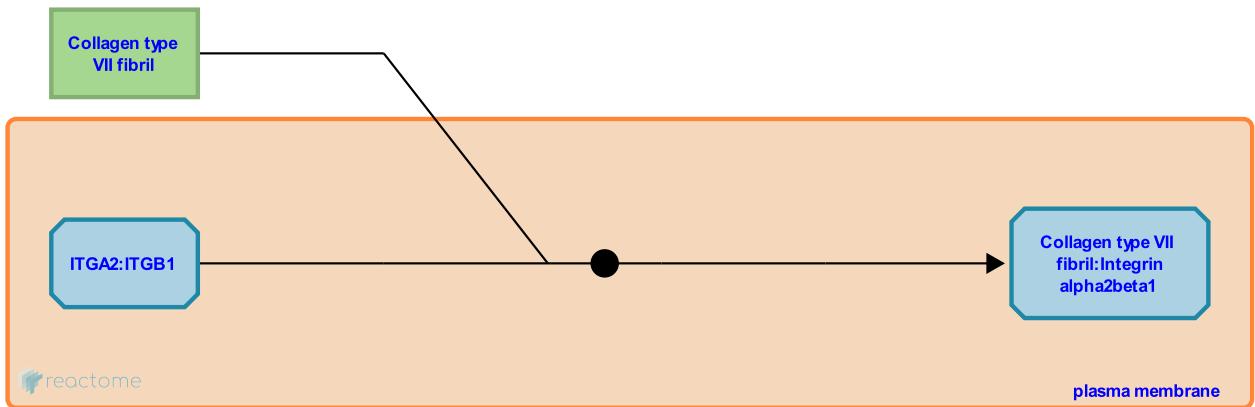
**Collagen type VII binds integrin alpha2beta1** ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4086216

**Type:** binding

**Compartments:** plasma membrane, extracellular region



The NC1 domains of collagen types VII (Chen et al. 1999) and X (Luckman et al. 2003) interact with integrin alpha2beta1.

**Literature references**

Li, YY., O'Toole, EA., Chen, M., Woodley, DT. (1999). Alpha 2 beta 1 integrin mediates dermal fibroblast attachment to type VII collagen via a 158-amino-acid segment of the NC1 domain. *Exp. Cell Res.*, 249, 231-9. ↗

**Editions**

2012-08-08	Authored	Jupe, S.
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2013-08-13	Reviewed	Ricard-Blum, S.

Collagen type X binds Integrin alpha2beta1 ↗

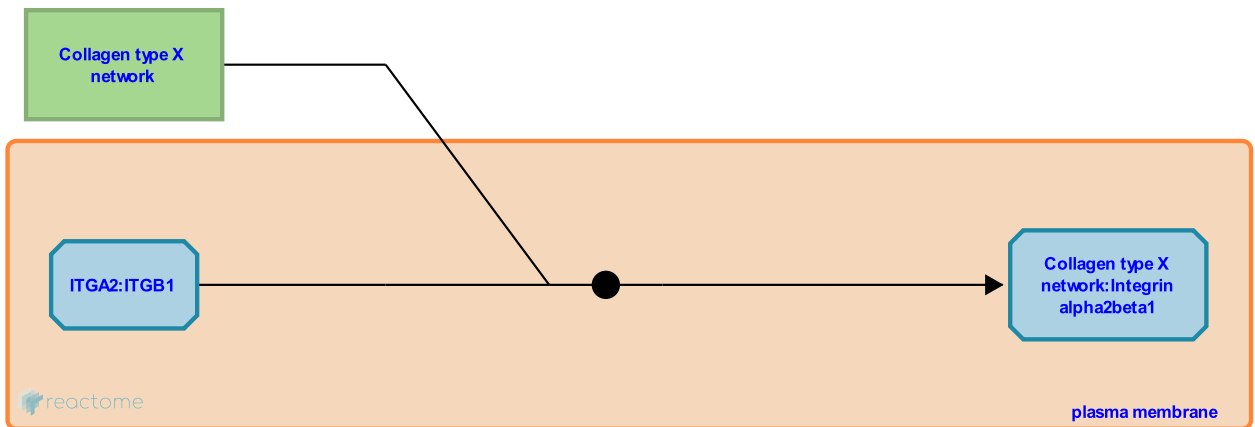
Location: [Integrin cell surface interactions](#)

Stable identifier: R-HSA-2470555

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: [Collagen type X binds integrin alpha2beta1 \(Homo sapiens\)](#)



The NC1 domains of collagen types VII (Chen et al. 1999) and X (Luckman et al. 2003) interact with integrin alpha2beta1. During endochondrial ossification, collagen type X is deposited in the hypertrophic zone of the growth plate. It interacts directly with chondrocytes via integrin alpha2beta1 (Luckman et al. 2003).

Editions

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2013-08-13	Reviewed	Ricard-Blum, S.

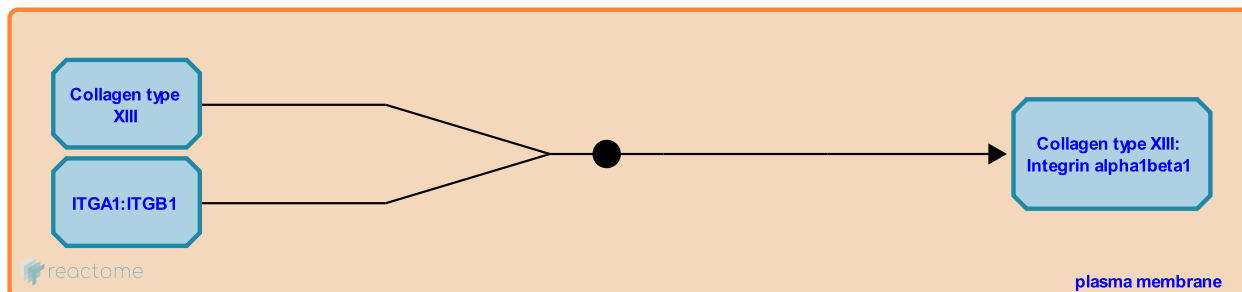
## Collagen type XIII binds Integrin alpha1beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-2484965

**Type:** binding

**Compartments:** plasma membrane



Integrin alpha1beta1 is a negative feedback regulator of collagen synthesis (Gardner et al. 1999). CHO cells expressing human integrin alpha1beta1, but not cells expressing integrin alpha2beta1, were able to bind recombinant human collagen type XIII, promoting cell spreading (Nykvist et al. 2000).

### Literature references

Nykvist, P., Heino, J., Pihlajaniemi, T., Käpylä, J., Ivaska, J., Tu, H. (2000). Distinct recognition of collagen subtypes by alpha(1)beta(1) and alpha(2)beta(1) integrins. Alpha(1)beta(1) mediates cell adhesion to type XIII collagen. *J Biol Chem*, 275, 8255-61. ↗

### Editions

2012-08-08	Authored	Jupe, S.
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2013-08-13	Reviewed	Ricard-Blum, S.

# Collagen type XXIII binds Integrin alpha2beta1 ↗

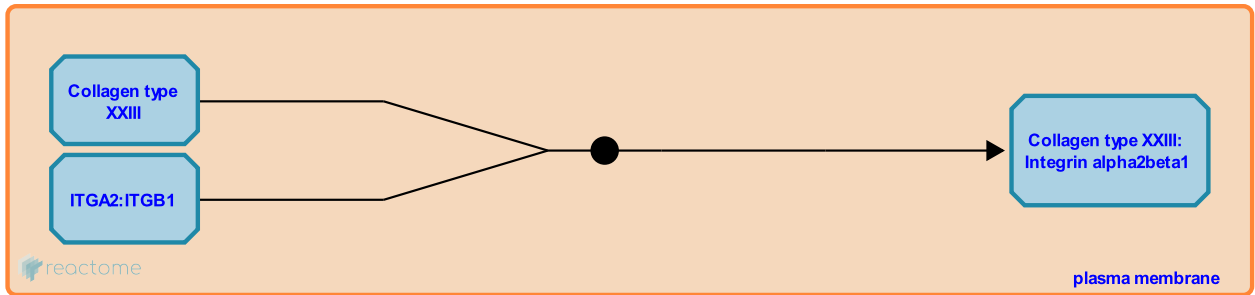
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-2473511

**Type:** binding

**Compartments:** plasma membrane

**Inferred from:** [Collagen type XXIII binds Integrin alpha2beta1 \(Homo sapiens\)](#)



Collagen type XXIII, a transmembrane collagen, binds integrin alpha2beta1, the only collagen-binding integrin present in the epidermis, in an ion- and conformation-dependent manner. Binding is sufficient to induce integrin alpha2beta1-dependent attachment and spreading of keratinocytes (Veit et al. 2007, 2011).

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2012-08-08	Authored	Jupe, S.
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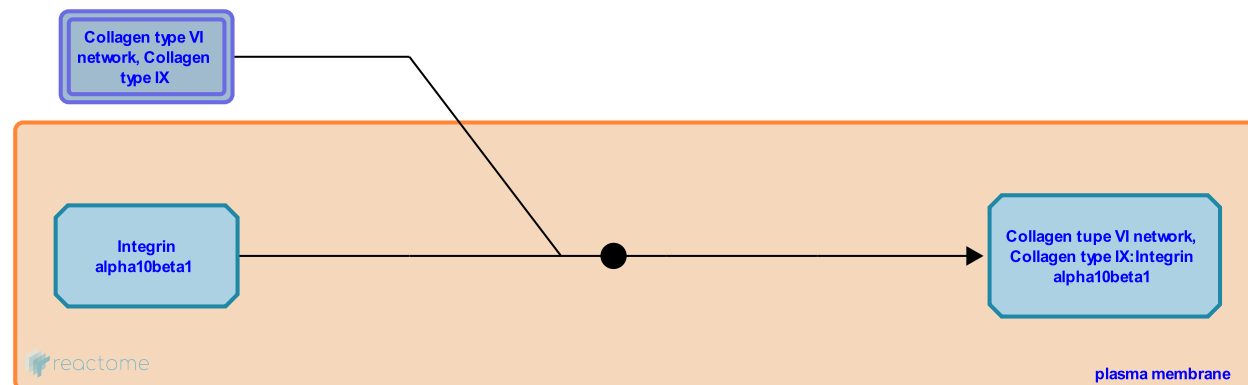
## Collagen types VI, IX bind integrin alpha10beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4084903

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Integrin alpha10beta1 binds collagen types I, IV, and VI with similar affinities (Tulla et al. 2001) and also collagen IX (Kapyla et al. 2004).

### Literature references

Nissinen, L., Jääliñoja, J., Heino, J., Vehviläinen, P., Farndale, RW., Viitasalo, T. et al. (2004). The fibril-associated collagen IX provides a novel mechanism for cell adhesion to cartilaginous matrix. *J. Biol. Chem.*, 279, 51677-87. ↗

Nissinen, L., Nykvist, P., Johnson, MS., Impola, U., Viitasalo, T., Tulla, M. et al. (2001). Selective binding of collagen subtypes by integrin alpha 1I, alpha 2I, and alpha 10I domains. *J. Biol. Chem.*, 276, 48206-12. ↗

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2012-08-08	Authored	Jupe, S.
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**Collagen type IV binds integrin alpha10beta1** ↗

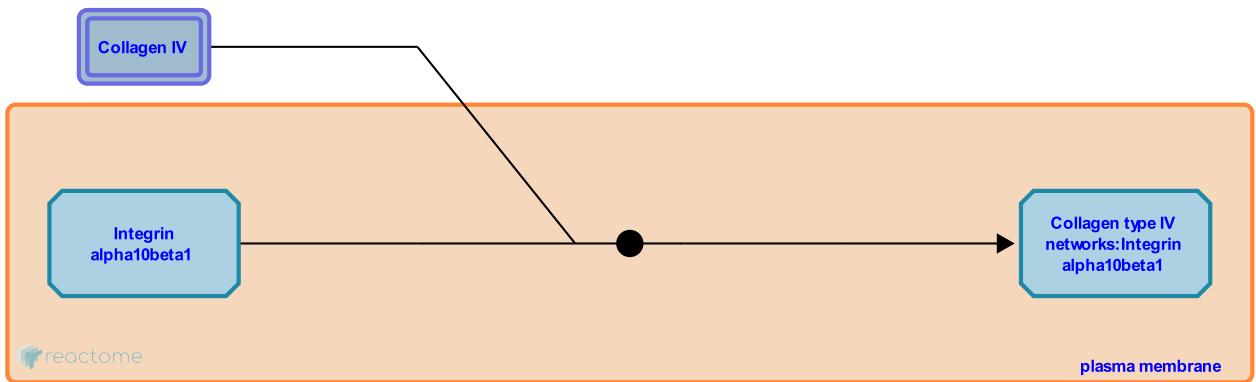
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4539779

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Inferred from:** [Collagen type IV binds integrin alpha10beta1 \(Homo sapiens\)](#)



Integrin alpha10beta1 binds collagen types I, IV and VI with similar affinities (Tulla et al. 2001).

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2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.



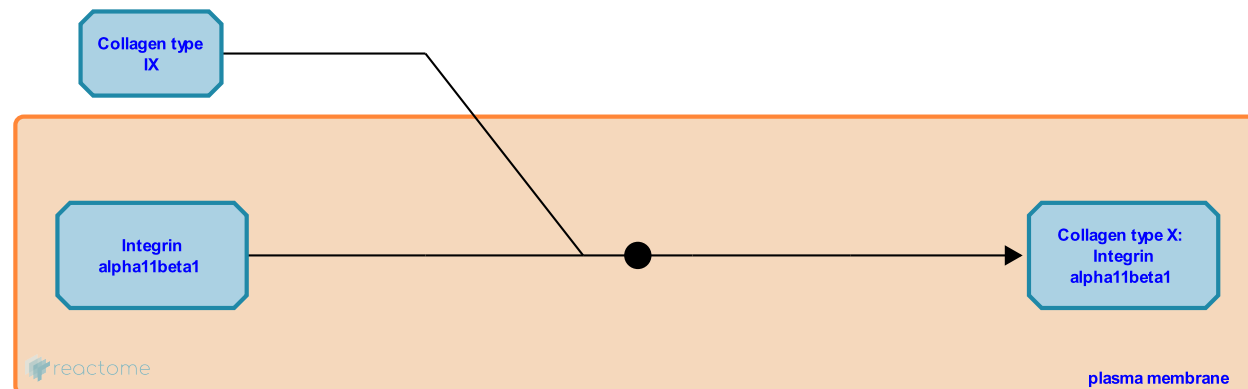
## Collagen type IX binds integrin alpha11beta1 [↗](#)

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4086223

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Collagen IX, expressed in cartilage and eye, is a high-avidity ligand for all four collagen receptor integrins including alpha11beta1.

### Literature references

Nissinen, L., Jääliñoja, J., Heino, J., Vehviläinen, P., Farndale, RW., Viitasalo, T. et al. (2004). The fibril-associated collagen IX provides a novel mechanism for cell adhesion to cartilaginous matrix. *J. Biol. Chem.*, 279, 51677-87. [↗](#)

### Editions

2012-08-08	Authored	Jupe, S.
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2013-08-13	Reviewed	Ricard-Blum, S.

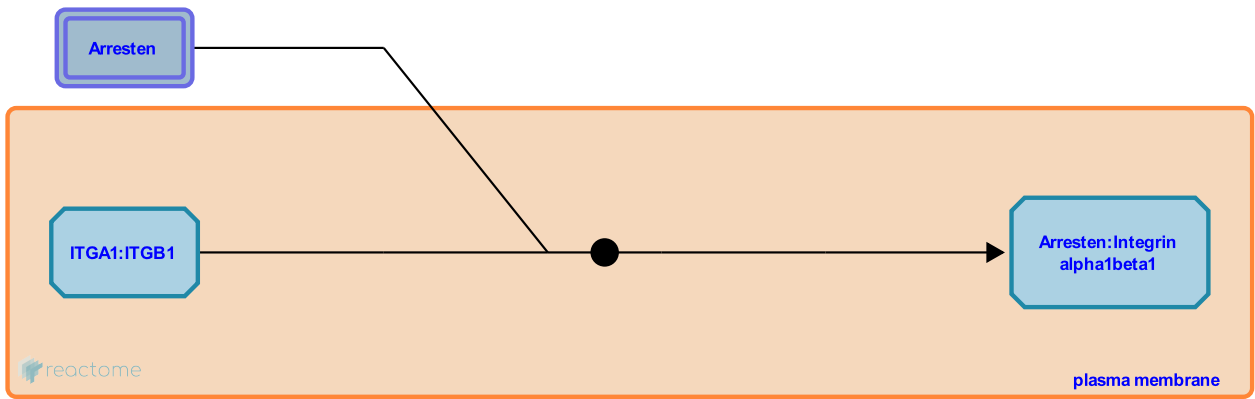
Arresten binds integrin alpha1beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4084912

**Type:** binding

**Compartments:** plasma membrane



Arresten, the non-collagenous domain (NC1) of alpha-1(IV) collagen, is a ligand for alpha1beta1 integrin (Colorado PC et al., 2000; Nyberg P et al., 2008). The interaction between arresten and alpha1beta1 integrin is supported by other studies (Aikio M et al., 2012; Zhu L et al., 2022)

Literature references

Sudhakar, A., Nyberg, P., Colorado, P., Kalluri, R., Sund, M., Holthaus, K. et al. (2008). Characterization of the anti-angiogenic properties of arresten, an alpha1beta1 integrin-dependent collagen-derived tumor suppressor. *Exp Cell Res*, 314, 3292-305. ↗

Kufe, DW., Takahashi, K., Colorado, PC., Weichselbaum, RR., Sarkar, PK., Simons, M. et al. (2000). Anti-angiogenic cues from vascular basement membrane collagen. *Cancer Res*, 60, 2520-6. ↗

Editions

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2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

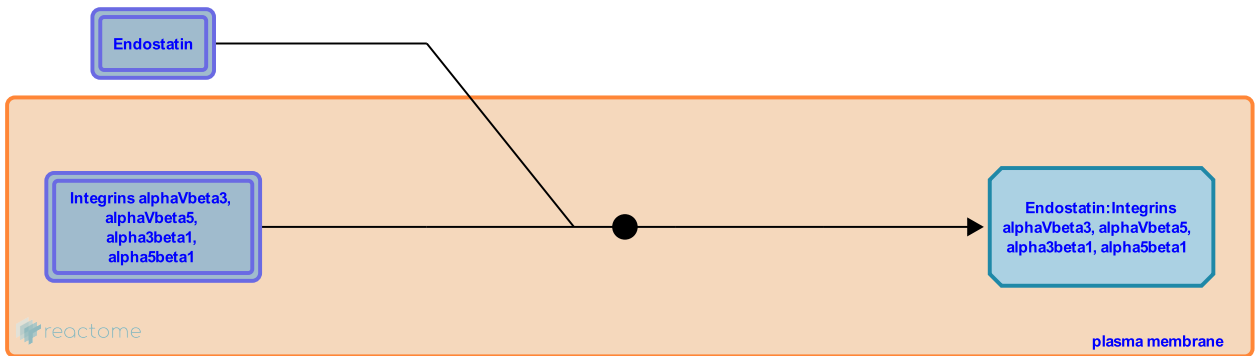
**Endostatin binds integrin alphaVbeta3, alphaVbeta5, alpha3beta1, alpha5beta1** [↗](#)

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4088264

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Endostatin binds to the integrins alphaVbeta3, alphaVbeta5, alpha5beta1 (Rehn et al. 2001, Faye et al. 2009) and alpha3beta1 (Su et al. 2012). Endostatin is the cleaved non-collagenous C terminal domain of collagen alpha-1(XVIII) a member of the multiplexin family. It inhibits endothelial cell migration, proliferation, and angiogenesis (Fu et al. 2009).

**Literature references**

Moreau, C., Olsen, BR., Ruggiero, F., Chautard, E., Humphries, MJ., Jetne, R. et al. (2009). Molecular interplay between endostatin, integrins, and heparan sulfate. *J. Biol. Chem.*, 284, 22029-40. [↗](#)

Stenbjorn, RS., Pihlajaniemi, T., Gorse, K., Su, J., Fox, MA., Su, K. et al. (2012). Target-derived matricryptins organize cerebellar synapse formation through  $\alpha 3 \beta 1$  integrins. *Cell Rep*, 2, 223-30. [↗](#)

Rehn, M., Pihlajaniemi, T., Veikkola, T., Lombardo, C., Kukk-Valdre, E., Alitalo, K. et al. (2001). Interaction of endostatin with integrins implicated in angiogenesis. *Proc. Natl. Acad. Sci. U.S.A.*, 98, 1024-9. [↗](#)

**Editions**

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2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

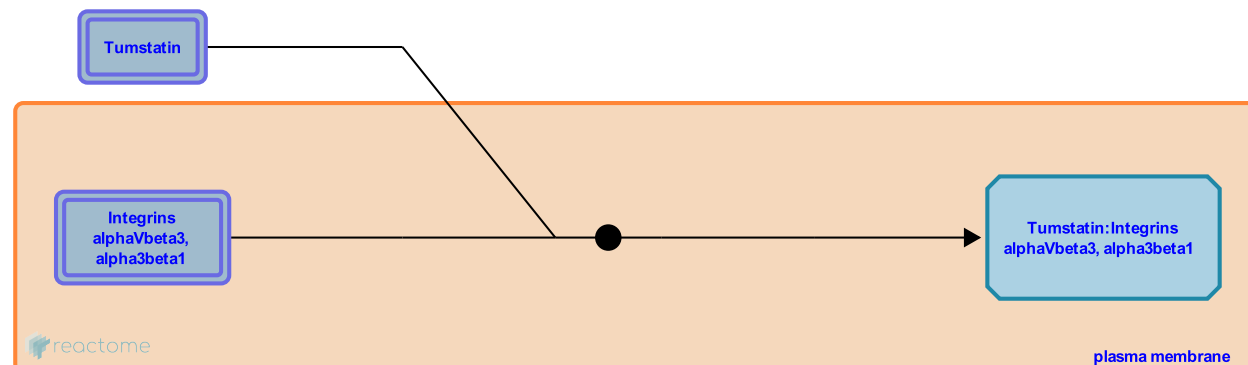
## Tumstatin binds integrin alphaVbeta 3, alpha3beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4085083

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Tumstatin, the non collagenous C-terminal domain of alpha-3(IV) collagen, binds to integrin alpha V beta 3 (Sudhakar et al. 2003) and alpha3beta1 (Borza et al. 2006).

### Literature references

Hudson, BG., Borza, DB., Zent, R., Borza, CM., Hellmark, T., Pozzi, A. et al. (2006). Integrin alpha3beta1, a novel receptor for alpha3(IV) noncollagenous domain and a trans-dominant Inhibitor for integrin alphavbeta3. *J. Biol. Chem.*, 281, 20932-9. ↗

Sudhakar, A., Yang, C., Lively, J., Kalluri, R., Sugimoto, H., Zeisberg, M. (2003). Human tumstatin and human endostatin exhibit distinct antiangiogenic activities mediated by alpha v beta 3 and alpha 5 beta 1 integrins. *Proc. Natl. Acad. Sci. U.S.A.*, 100, 4766-71. ↗

### Editions

2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

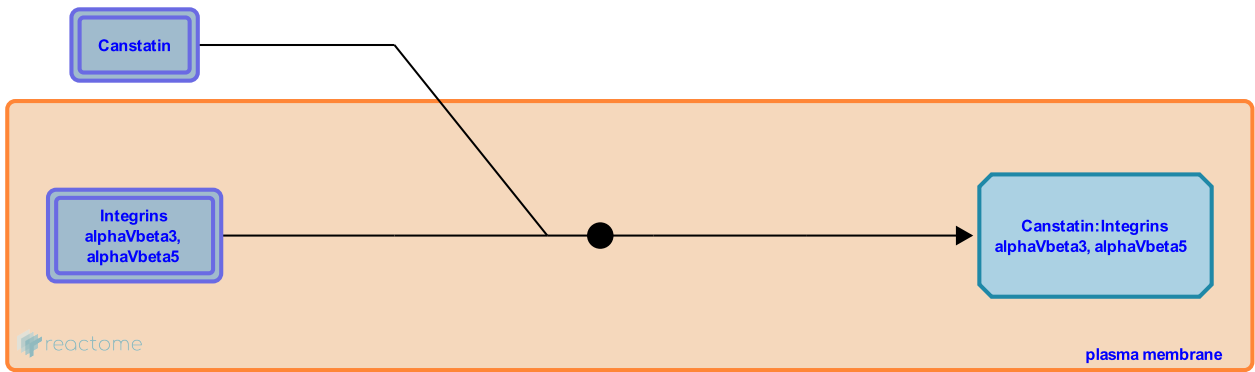
**Canstatin binds integrins alphaVbeta3, alphaVbeta5** ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4085087

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Canstatin is the non-collagenous C-terminal domain of alpha-2(IV) collagen. It is an inhibitor of endothelial and tumor cells via mitochondrial damage initiated through an interaction with integrins alphaVbeta3 and alphaVbeta5 (Magnon et al. 2005).

**Literature references**

Galaup, A., Perricaudet, M., Bouquet, C., Opolon, P., Bidart, JM., Magnon, C. et al. (2005). Canstatin acts on endothelial and tumor cells via mitochondrial damage initiated through interaction with alphavbeta3 and alphavbeta5 integrins. *Cancer Res.*, 65, 4353-61. ↗

**Editions**

2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

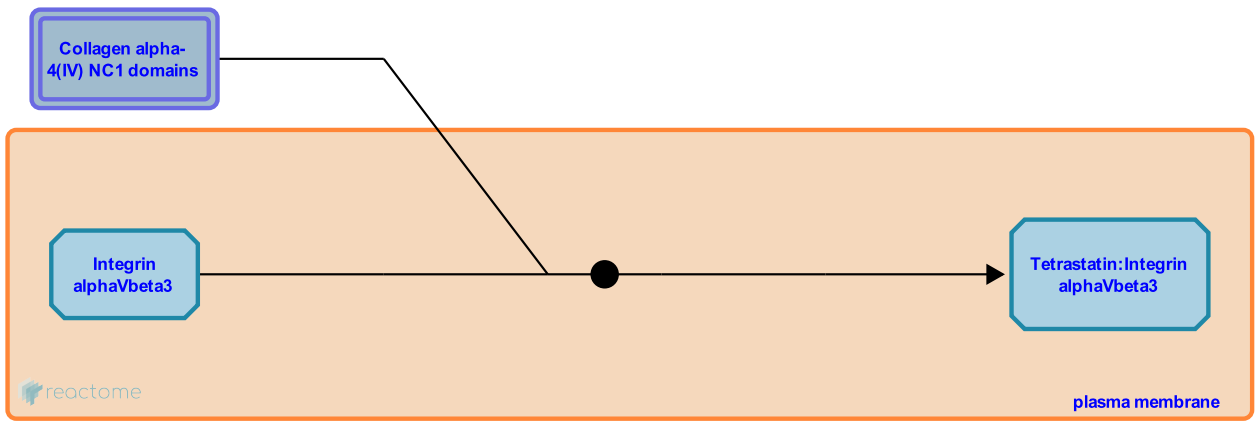
**Tetrastatin binds integrin alphaVbeta3** ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4088218

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Tetrastatin, the non-collagenous C-terminal domain of collagen alpha-4(IV) has anti-tumor activity in a human melanoma model, decreasing proliferative and invasive properties of melanoma cells. This effect is mediated by integrin alphaVBeta3.

**Literature references**

Brézillon, S., Di Stefano, L., Thevenard, J., Sénéchal, K., Devy, J., Jazeron, JF. et al. (2012). Tetrastatin, the NC1 domain of the  $\alpha$ 4(IV) collagen chain: a novel potent anti-tumor matrikine. *PLoS ONE*, 7, e29587. ↗

**Editions**

2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

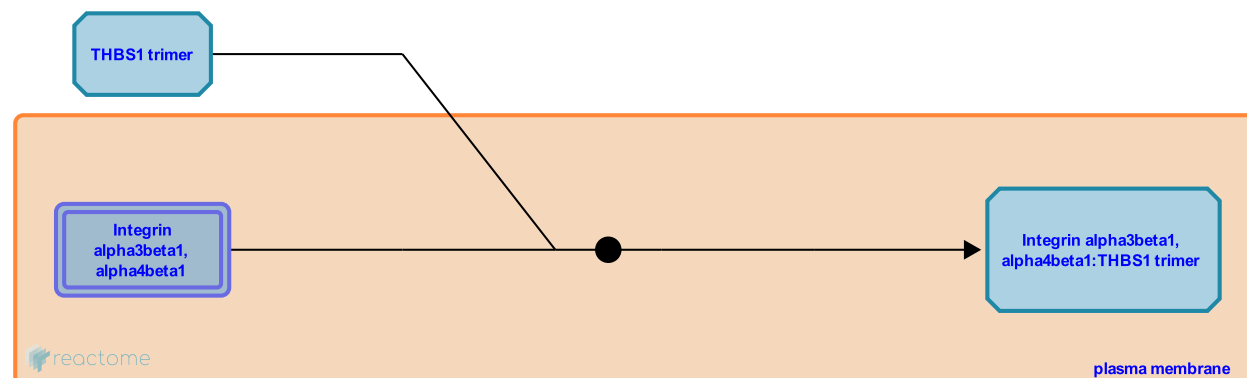
## THBS1 (Thrombospondin-1) binds Integrin alpha3beta1, alpha4beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-265429

**Type:** binding

**Compartments:** plasma membrane, extracellular region



The alpha3beta1 integrin is localized in cell-cell junctions of endothelial cells and this integrin is involved in regulating angiogenesis by interacting with thrombospondin-1 (TSP1). Alpha4beta1 integrin binds to the N-terminal pentraxin modules of TSP1 and stimulates chemotaxis and modulates T cell behavior both positively and negatively.

### Literature references

Krutzsch, HC., Chandrasekaran, L., Iruela-Arispe, ML., Al-Barazi, H., He, CZ., Roberts, DD. (2000). Cell contact-dependent activation of alpha3beta1 integrin modulates endothelial cell responses to thrombospondin-1. *Mol Biol Cell*, 11, 2885-900. ↗

Krutzsch, HC., Cashel, JA., Mosher, DF., Calzada, MJ., Li, Z., Annis, DS. et al. (2002). Interactions of thrombospondins with alpha4beta1 integrin and CD47 differentially modulate T cell behavior. *J Cell Biol*, 157, 509-19. ↗

### Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

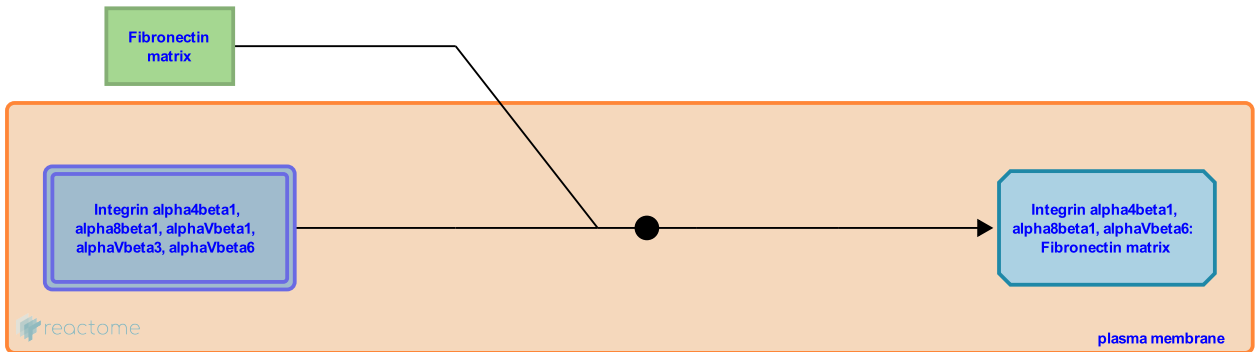
**Integrins alpha4beta1, alpha8beta1, alphaVbeta1, alphaVbeta3, alphaVbeta6 bind Fibronectin matrix ↗**

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216050

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Several integrins are able to bind fibronectin (FN1). Alpha5beta1 is a specialist FN1 receptor (Singh et al. 2010). The alpha4beta1 (VAL-4) integrin has been suggested to play an important role in haemopoiesis. Fibronectin and VCAM-1 are the main ligands for VLA-4. The H1 region present in all FN isoforms represents the binding site for VLA-4, alphaIIbBeta3, which is highly expressed on platelets where it predominantly binds fibrinogen leading to thrombus formation but also binds FN1 (Savage et al. 1996). Alpha4beta1 mediates cell-cell contacts and cell-matrix contacts through the ligands VCAM-1 and FN1, respectively (Humphries et al. 1995), this is suggested to play an important role in haemopoiesis. The H1 region present in all FN isoforms represents the binding site for VLA-4. Integrins alpha3beta1, alpha4beta7, alphaVbeta1, 3 (Wu et al. 1996, Johansson et al. 1997), 6 (Busk et al. 1992) and alpha8beta1 (Muller et al. 1995, Farias et al. 2005) are all able to bind FN1.

Tenacious binding of free fibronectin to cells leads to enhanced fibronectin matrix assembly and the formation of a polymerized fibronectin "cocoon" around the cells. This process is enhanced in the presence of CEACAM molecules.

**Literature references**

Garcia-Pardo, A., Brieva, JA., Roldán, E. (1992). VLA-4-fibronectin interaction is required for the terminal differentiation of human bone marrow cells capable of spontaneous and high rate immunoglobulin secretion. *J Exp Med*, 175, 1739-47. ↗

Ishikawa, J., Karasuno, T., Nishiura, T., Matsuzawa, Y., Yokota, T., Yoshimura, M. et al. (1998). Effect of the interaction between fibronectin and VLA-4 on the proliferation of human B cells, especially a novel human B-cell line, OPM-3. *Br J Haematol*, 103, 804-12. ↗

**Editions**

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.



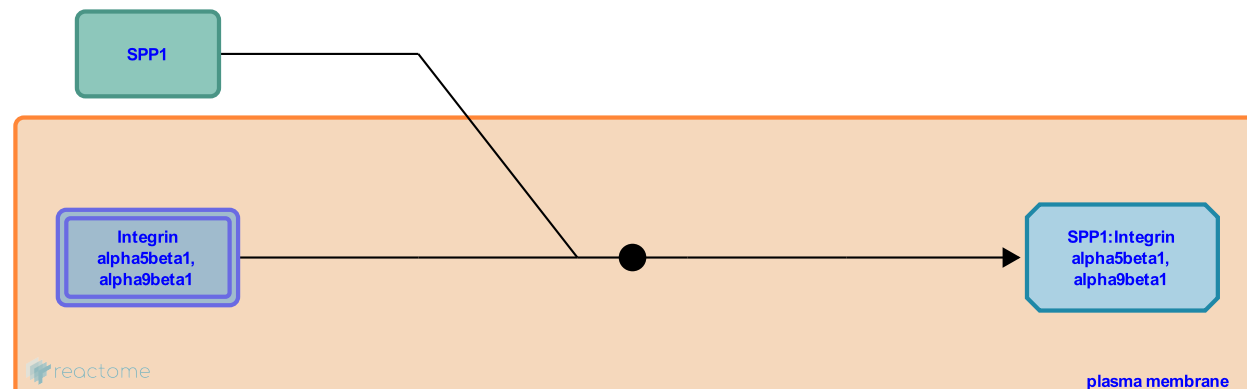
## SPP1 (osteopontin) binds integrin alpha5beta1, alpha9beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-265424

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Osteopontin (SPP1) is a highly phosphorylated sialoprotein that is a prominent component of the mineralized extracellular matrices of bones and teeth. It provides an adhesive matrix for endothelial and smooth muscle cells during remodeling of the vascular wall following injury. SPP1 binds multiple integrins including alphaVbeta3, alphaVbeta1 and alphaVbeta5 (Liaw et al. 1995), alpha5beta1 (Barry et al. 2000), alpha9beta1 (Smith et al. 1996, Yokosaki et al. 1999) alpha4beta1 (Bayless et al. 1998), alpha8beta1 (Denda et al. 1998) and the receptor CD44 (Katagiri et al. 1999). Integrin alpha4beta1 is expressed on leukocytes, differentiated vascular smooth muscle cells and tumor cells. It has been shown to mediate leukocyte attachment to OPN.

### Literature references

- Horgan, CM., Murrison, E., Barry, ST., Ludbrook, SB. (2000). A regulated interaction between alpha5beta1 integrin and osteopontin. *Biochem Biophys Res Commun*, 267, 764-9. ↗
- Giachelli, CM., Ling, LE., Cheung, HK., Pytela, R., Chen, J., Smith, LL. et al. (1996). Osteopontin N-terminal domain contains a cryptic adhesive sequence recognized by alpha9beta1 integrin. *J Biol Chem*, 271, 28485-91. ↗
- Yamakido, M., Sasaki, T., Saitoh, Y., Murakami, I., Matsuura, N., Taooka, Y. et al. (1999). The integrin alpha(9)beta(1) binds to a novel recognition sequence (SVVYGLR) in the thrombin-cleaved amino-terminal fragment of osteopontin. *J Biol Chem*, 274, 36328-34. ↗

### Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.
2013-08-13	Revised	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

**SPP1 (osteopontin) binds Integrin alpha4beta1** ➤

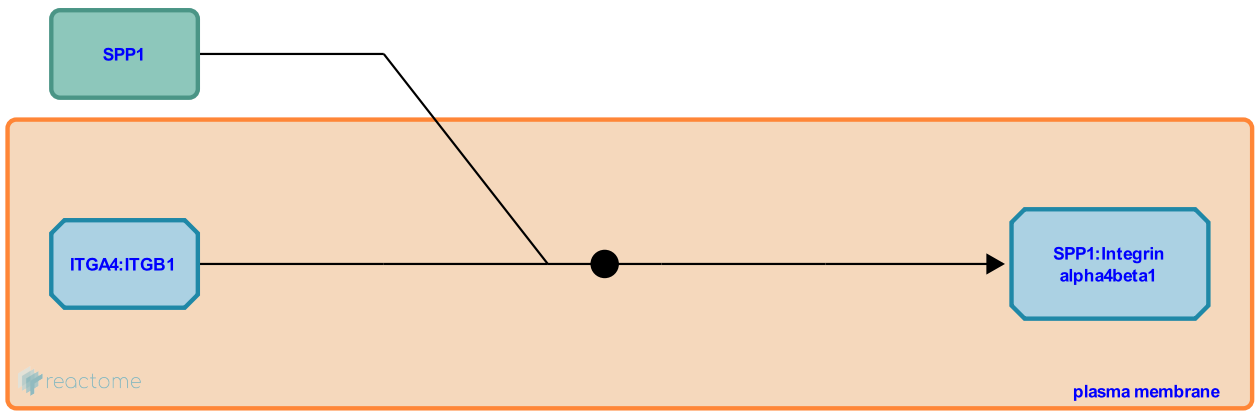
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-2752118

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Inferred from:** [Osteopontin binds Integrin alpha4beta1 \(Homo sapiens\)](#)



Osteopontin (SPP1) is a highly phosphorylated sialoprotein that is a prominent component of the mineralized extracellular matrices of bones and teeth. It provides an adhesive matrix for endothelial and smooth muscle cells during remodeling of the vascular wall following injury. SPP1 binds multiple integrins including alphaVbeta3, alphaVbeta1 and alphaVbeta5 (Liaw et al. 1995), alpha5beta1 (Barry et al. 2000), alpha9beta1 (Smith et al. 1996, Yokosaki et al. 1999) alpha4beta1 (Bayless et al. 1998), alpha8beta1 (Denda et al. 1998) and the receptor CD44 (Katagiri et al. 1999). Integrin alpha4beta1 is expressed on leukocytes, differentiated vascular smooth muscle cells and tumor cells. It has been shown to mediate leukocyte attachment to OPN.

**Editions**

2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

**SPP1 (osteopontin) binds integrin alpha8beta1** ↗

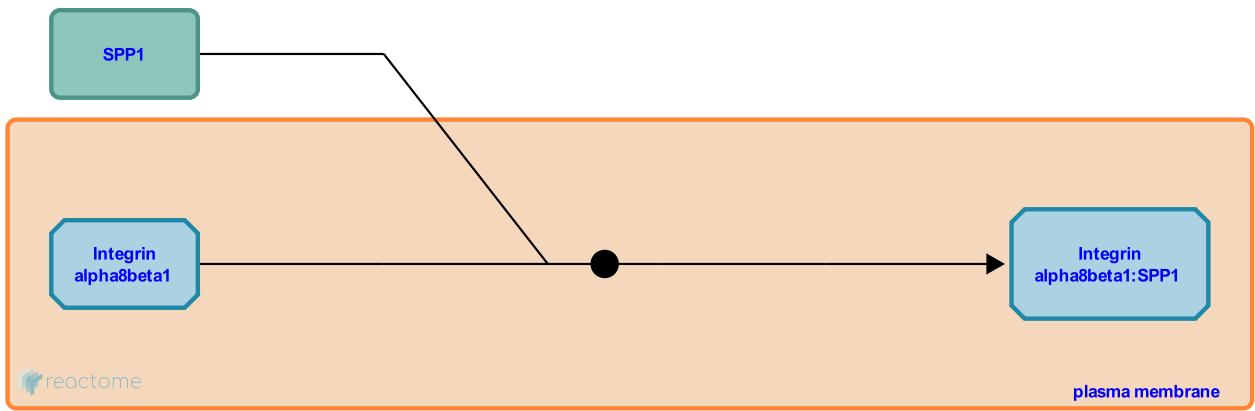
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216061

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Inferred from:** [Osteopontin binds integrin alpha8beta1 \(Mus musculus\)](#)



Osteopontin (SPP1) is a highly phosphorylated sialoprotein that is a prominent component of the mineralized extracellular matrices of bones and teeth. It binds multiple integrins, including alphaVbeta3, alphaVbeta1 and alphaVbeta5 (Liaw et al. 1995) alpha9beta1 (Smith et al. 1996, Yokosaki et al. 1999), alpha4beta1 (Bayliss et al. 1998), alpha8beta1 (Denda et al. 1998) and the receptor CD44 (Katagiri et al. 1999).

**Editions**

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.
2013-08-13	Revised	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

**SPP1 (osteopontin) binds integrins alphaVbeta1, alphaVbeta3, alphaVbeta5** ↗

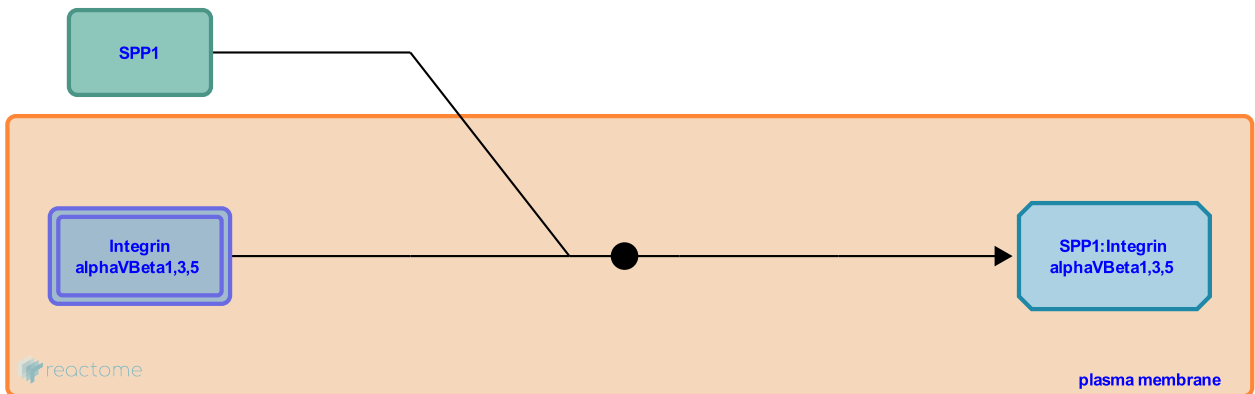
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-2752125

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Inferred from:** [Osteopontin binds Integrins alphaVbeta1, 3, 5 \(Homo sapiens\)](#)



Osteopontin (SPP1) is a highly phosphorylated sialoprotein that is a prominent component of the mineralized extracellular matrices of bones and teeth. It binds multiple integrins, including alphaVbeta3, alphaVbeta1 and alphaVbeta5 (Liaw et al. 1995) alpha9beta1 (Smith et al. 1996, Yokosaki et al. 1999), alpha4beta1 (Bayliss et al. 1998) and the receptor CD44 (Katagiri et al. 1999).

**Editions**

2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

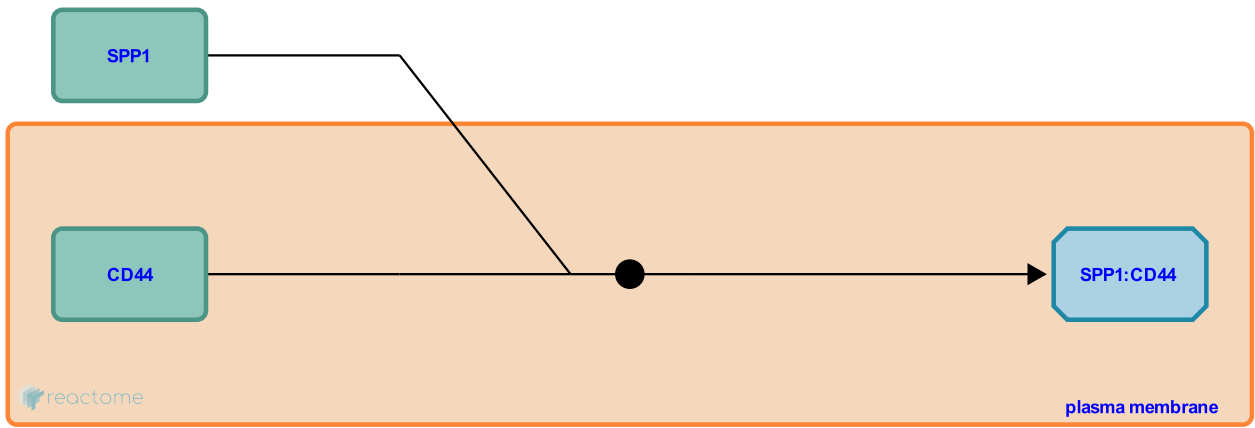
**SPP1 (osteopontin) binds CD44** ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-2752115

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Osteopontin (SPP1) is a member of the small integrin-binding ligand N-linked glycoprotein (SIBLING) family of proteins (Bellahcène et al. 2008). It is a highly phosphorylated sialoprotein and prominent component of the mineralized extracellular matrices of bones and teeth. It binds multiple integrins including alphaVbeta3, alphaVbeta1 and alphaVbeta5 (Liaw et al. 1995) alpha9beta1 (Smith et al. 1996, Yokosaki et al. 1999), alpha4beta1 (Bayliss et al. 1998) and the receptor CD44 (Weber et al. 1996, Katagiri et al. 1999). The SPP1–CD44 interaction may be important for colorectal cancer progression (Rao et al. 2013).

**Literature references**

Ashkar, S., Cantor, H., Glimcher, MJ., Weber, GF. (1996). Receptor-ligand interaction between CD44 and osteopontin (Eta-1). *Science*, 271, 509-12. ↗

**Editions**

2012-07-31	Authored	Jupe, S.
2013-04-26	Edited	Jupe, S.
2013-05-22	Reviewed	Ricard-Blum, S.

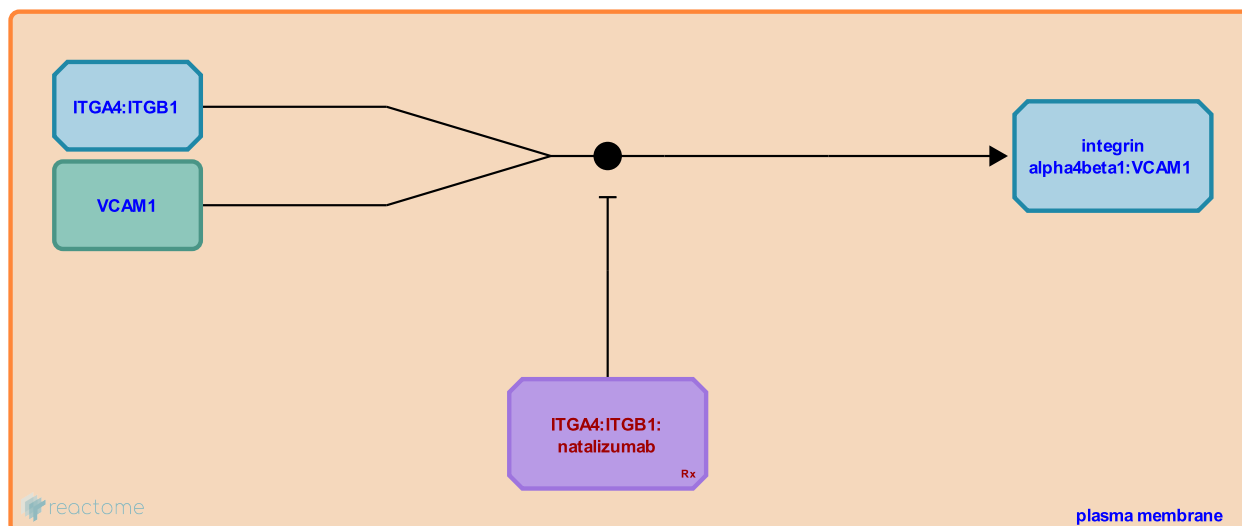
## VCAM1 binds Integrin alpha4beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-198941

**Type:** binding

**Compartments:** plasma membrane



Integrins play a central role in mediating lymphocyte adhesion to a number of surfaces. Integrin alphaLbeta2 (LFA-1) interacts with Intercellular adhesion molecule (ICAM)1-5, which are typically expressed on other immune system cells. ICAM4 and 5 are known to be expressed on telencephalic neurons. VCAM-1 regulates lymphocyte adhesion to activated endothelial cells via Very Late Antigen-4 (VLA-4). To function in a circulating mode, leukocytes express LFA-1 and VLA-4 in a low ligand binding capacity. When leukocytes reach sites of inflammation, these integrins are switched to a higher binding state to guide the complex process of transmigration, tethering, rolling, arrest, adhesion and shape change. Signal cascades between LFA-1 and VLA-4 may cross-talk affecting binding affinities in a reciprocal fashion.

### Literature references

Clements, JM., Harlos, K., Jones, EY., Dudgeon, TJ., Bottomley, MJ., Edwards, RM. et al. (1995). Crystal structure of an integrin-binding fragment of vascular cell adhesion molecule-1 at 1.8 Å resolution. *Nature*, 373, 539-44. ↗

Yusuf-Makagiansar, H., Murray, JS., Siahaan, TJ., Anderson, ME., Yakovleva, TV. (2002). Inhibition of LFA-1/ICAM-1 and VLA-4/VCAM-1 as a therapeutic approach to inflammation and autoimmune diseases. *Med Res Rev*, 22, 146-67. ↗

### Editions

2007-07-08	Authored	de Bono, B.
2007-08-06	Reviewed	Trowsdale, J.
2015-05-13	Reviewed	Barrow, AD.

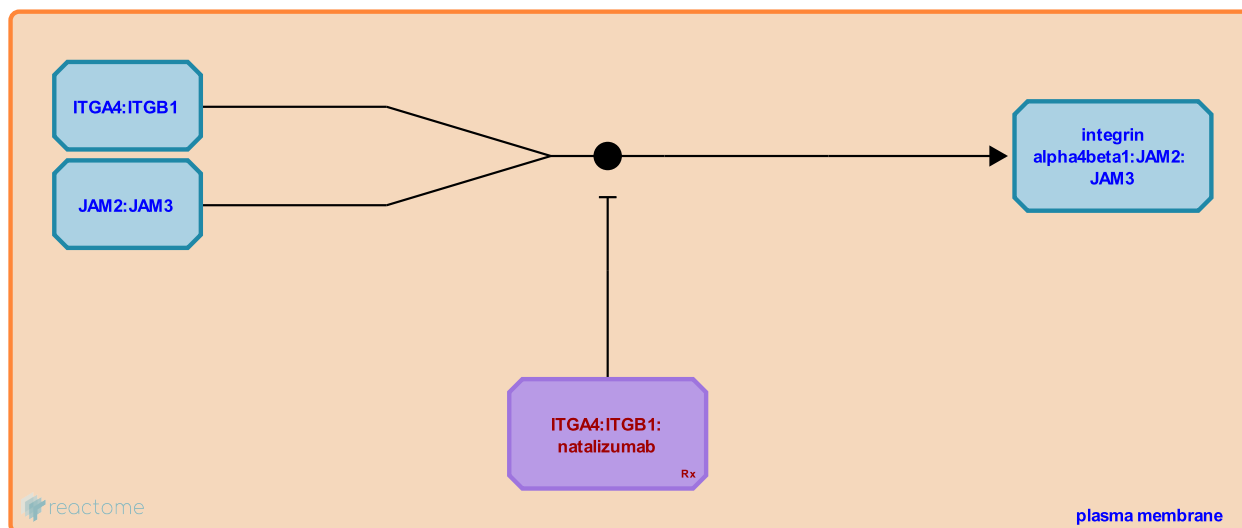
## Integrin alpha4beta1 binds JAM2:JAM3 [↗](#)

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-202706

**Type:** binding

**Compartments:** plasma membrane



Several key IgSF cell adhesion molecules engage integrin and in so doing impact on the multi-step paradigm of leukocyte emigration. The interaction between JAM2 (JAM-B) and Integrin alpha4beta1 (VLA-4) requires prior binding of JAM2 to JAM3 (JAM-C).

### Literature references

Tran, TM., Brock, TA., Cunningham, SA., Rodriguez, JM., Arrate, MP. (2002). JAM2 interacts with alpha4beta1. Facilitation by JAM3. *J Biol Chem*, 277, 27589-92. [↗](#)

Weber, C., Fraemohs, L., Dejana, E. (2007). The role of junctional adhesion molecules in vascular inflammation. *Nat Rev Immunol*, 7, 467-77. [↗](#)

### Editions

2007-11-12	Authored	Ouwehand, WH.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

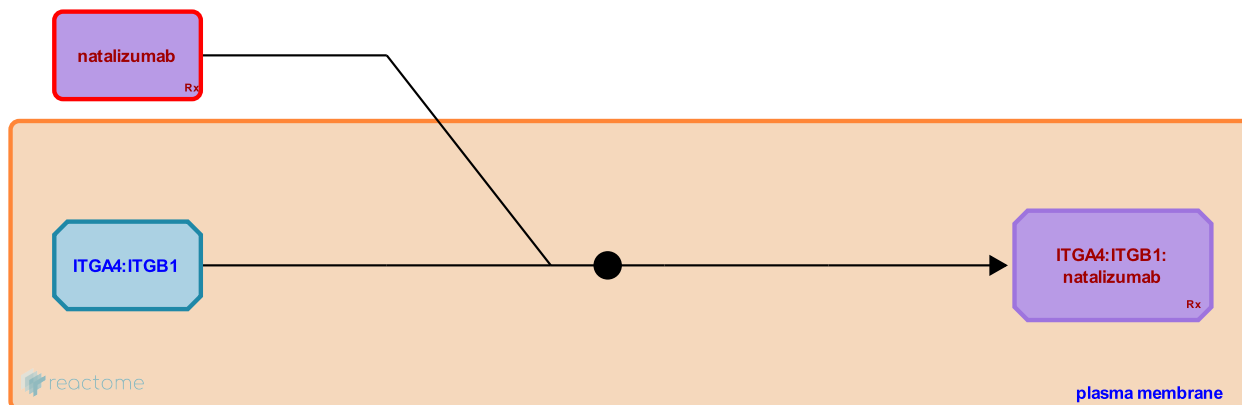
## ITGA4:ITGB1 binds natalizumab ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-9679740

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Integrins are the receptors that mediate cell adhesion to the extracellular matrix (ECM). They are involved in cell adhesion and recognition in a variety of processes including embryogenesis, hemostasis, tissue repair, immune response and metastatic diffusion of tumor cells. Integrin alpha-4 (ITGA4) is a receptor for fibronectin. ITGA4 functions as a heterodimer of an alpha subunit and the beta subunit of either the beta-1 chain or the beta-7 chain (ITGA4:ITGB1 shown here).

Natalizumab (Tysabri) is a humanised monoclonal antibody against the cell adhesion molecule  $\alpha$ 4-integrin. It is a medication used to treat multiple sclerosis and Crohn's disease (No authors 2004). It binds to the  $\alpha$ 4-subunit of  $\alpha$ 4b1 and  $\alpha$ 4b7 integrins expressed on the surface of all leukocytes except neutrophils, and inhibits the  $\alpha$ 4-mediated adhesion of leukocytes to their counter-receptors. This is thought to reduce the ability of inflammatory immune cells to attach to and pass through the cell layers lining the intestines and blood–brain barrier (Rice et al. 2005).

### Literature references

Hartung, HP., Calabresi, PA., Rice, GP. (2005). Anti-alpha4 integrin therapy for multiple sclerosis: mechanisms and rationale. *Neurology*, 64, 1336-42. ↗

### Editions

2020-03-25	Authored, Edited	Jassal, B.
2020-05-14	Reviewed	Shoichet, BK.



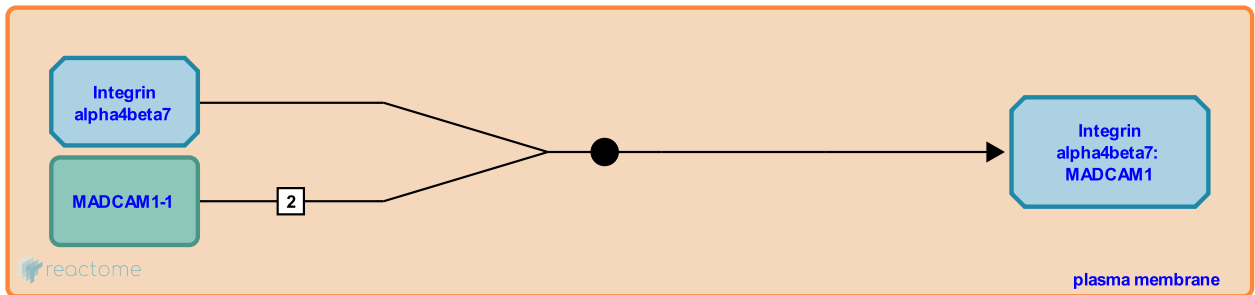
# MADCAM1-1 binds Integrin alpha4beta7 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-199032

**Type:** binding

**Compartments:** plasma membrane



Mucosal addressin cell adhesion molecule (MADCAM1) is present in the endothelium of mucosa, and binds alpha-4 beta-7 integrin and L-selectin, regulating both the passage and retention of leukocytes in mucosal tissues. MADCAM1 has been shown to be present as a homodimer.

## Literature references

Springer, TA., Wang, J. (1998). Structural specializations of immunoglobulin superfamily members for adhesion to integrins and viruses. *Immunol Rev*, 163, 197-215. ↗

King, DJ., Brady, RL., Dando, J., Ortlepp, S., Wilkinson, KW. (2002). A reassessment of the MADCAM-1 structure and its role in integrin recognition. *Acta Crystallogr D Biol Crystallogr*, 58, 233-41. ↗

## Editions

2007-07-08	Authored	de Bono, B.
2007-08-06	Reviewed	Trowsdale, J.
2015-05-13	Reviewed	Barrow, AD.

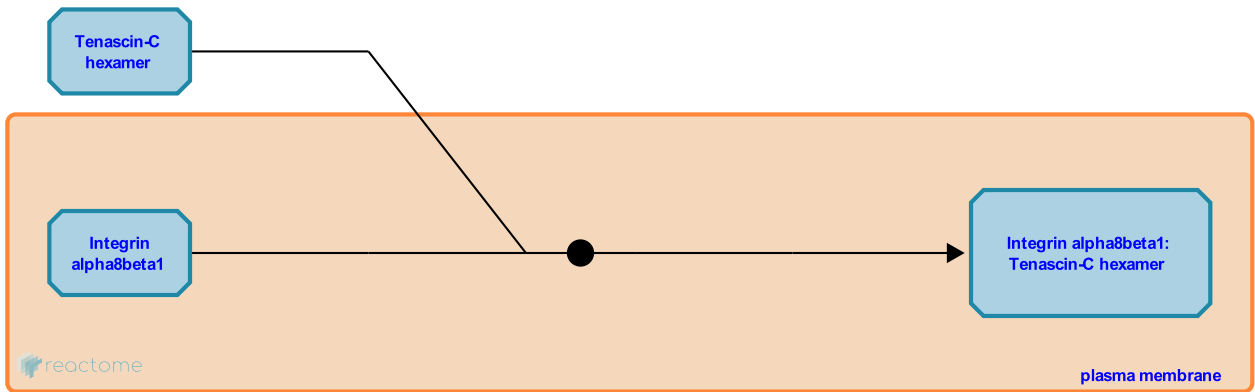
# Interaction of integrin alpha8beta1 with Tenascin-C ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216064

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Tenascin-C (TN-C) and its isoforms are multidomain extracellular matrix (ECM) proteins that are believed to be involved in the regulation of stromal-epithelial interactions. Some of the interactions between TN-C and cells are mediated by integrins. Alpha8beta1 integrin interacts with the third FN type III repeats which contains an RGD sequence in tenascin-c.

## Literature references

Chiquet, M., Backus, C., Kypta, R., Muller, U., Varnum-Finney, B., Venstrom, K. et al. (1995). The integrin receptor alpha 8 beta 1 mediates interactions of embryonic chick motor and sensory neurons with tenascin-C. *Neuron*, 14, 1213-22. ↗

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

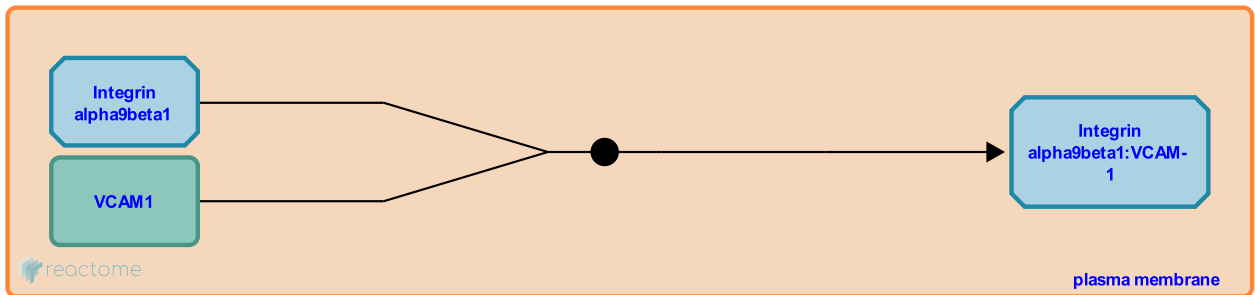
# Interaction of integrin alpha9beta1 with VCAM1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-265428

**Type:** binding

**Compartments:** plasma membrane



Integrin alpha9beta1 is widely expressed on smooth muscle, epithelial cells, and highly and specifically expressed on neutrophils. VCAM-1 is one of the effective ligands for the integrin alpha9beta1. This interaction mediates the neutrophil migration on VCAM-1 and extravasation of neutrophils at sites of acute inflammation.

## Literature references

Yednock, T., Taooka, Y., Sheppard, D., Chen, J. (1999). The integrin alpha9beta1 mediates adhesion to activated endothelial cells and transendothelial neutrophil migration through interaction with vascular cell adhesion molecule-1. *J Cell Biol*, 145, 413-20. ↗

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

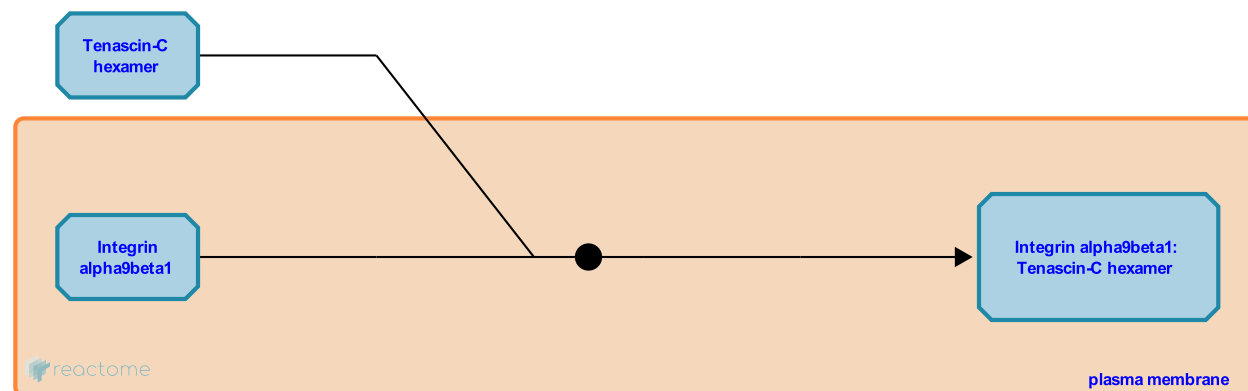
## Interaction of integrin alpha9beta1 with Tenascin-C ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216068

**Type:** binding

**Compartments:** plasma membrane, extracellular region



The integrin alpha 9 subunit forms a single heterodimer, alpha9beta1 that mediates cell adhesion to a site within the third fibronectin type III repeat of tenascin-C.

### Literature references

Yamakido, M., Murakami, I., Obara, M., Matsuura, N., Higashiyama, S., Shigeto, N. et al. (1998). Identification of the ligand binding site for the integrin alpha9 beta1 in the third fibronectin type III repeat of tenascin-C. *J Biol Chem*, 273, 11423-8. ↗

### Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

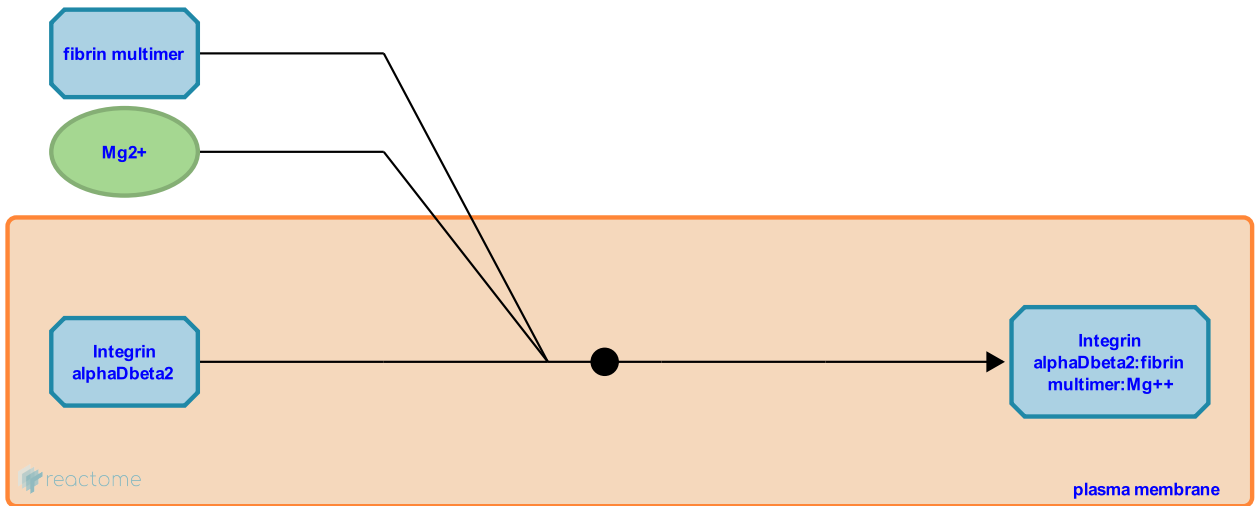
# Interaction of integrin alphaDbeta2 with fibrin ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216069

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Integrin alphaDbeta2 is a member of the beta2 family. It is expressed poorly on peripheral blood leukocytes but strongly on macrophages. alphaDbeta2 has the ability to interact with multiple ligands, including many ECM proteins. The interaction of beta2 integrins with ligands is mediated by their I-domains of the alpha subunits. The alphaD I-domain mediates the interaction with the ECM protein fibrinogen.

## Literature references

Van der Vieren, M., Gallatin, WM., Staunton, DE., Bochner, BS., Hoffman, PA., Vazeux, R. et al. (1999). The leukocyte integrin alpha D beta 2 binds VCAM-1: evidence for a binding interface between I domain and VCAM-1. *J Immunol*, 163, 1984-90. ↗

Ugarova, TP., Yadav, SP., Yakubenko, VP. (2006). Integrin alphaDbeta2, an adhesion receptor up-regulated on macrophage foam cells, exhibits multiligand-binding properties. *Blood*, 107, 1643-50. ↗

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

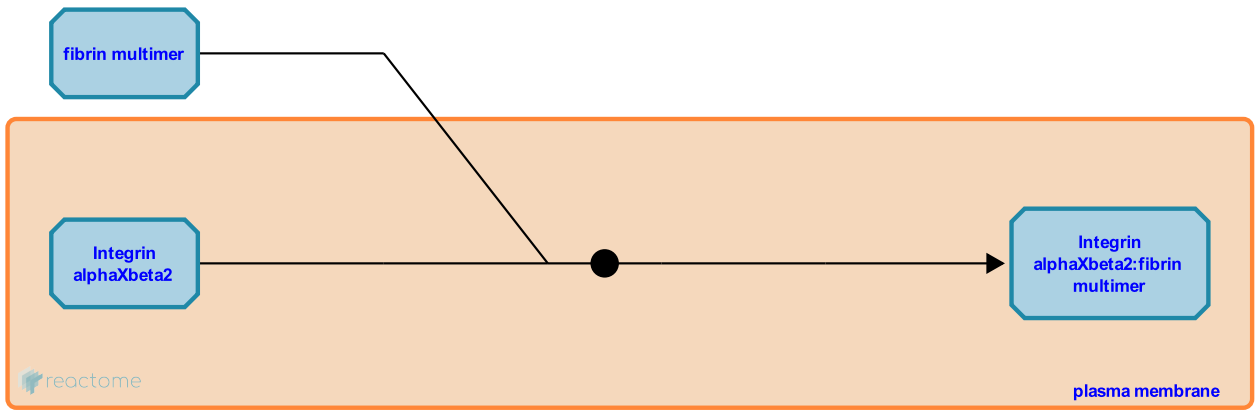
# Interaction of integrin alphaXbeta2 with fibrin [↗](#)

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216082

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Integrin alphaXbeta2 serves as a cell surface receptor for fibrinogen and plays an important role in leukocyte functions including phagocytosis and migration.

## Literature references

Nham, SU. (1999). Characteristics of fibrinogen binding to the domain of CD11c, an alpha subunit of p150,95. *Biochem Biophys Res Commun*, 264, 630-4. [↗](#)

Choi, J., Nham, SU., Lee, JH. (2007). Critical residues of alphaX I-domain recognizing fibrinogen central domain. *Biochem Biophys Res Commun*, 355, 1058-63. [↗](#)

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

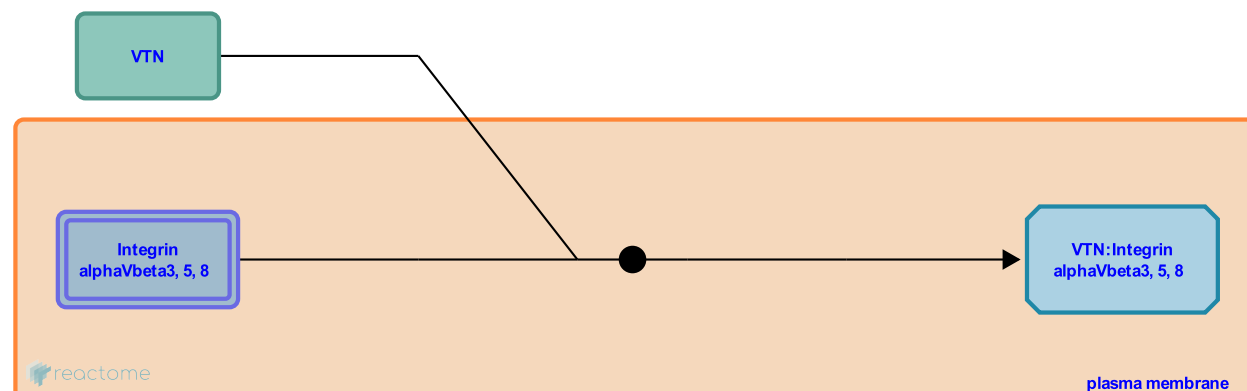
## VTN (vitronectin) binds Integrin alphaVbeta3, alphaVbeta5, alphaVbeta8 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216076

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Integrin alphaVbeta3 is highly expressed on osteoclasts, bone resorbing cells and is upregulated during vascular damage, angiogenesis and certain type of malignancies. It binds to vitronectin by recognizing the conserved RGD sequence within the N-terminal region. Integrin alphaVbeta3 plays an important role in signal transduction and regulation of osteoclast function. The integrin alphaVbeta5 receptor also interacts with vitronectin, promoting cell spreading. Integrin alphaVbeta8 can bind vitronectin as well as fibrin.

### Literature references

- Panetti, TS., McKeown-Longo, PJ. (1993). The alpha v beta 5 integrin receptor regulates receptor-mediated endocytosis of vitronectin. *J. Biol. Chem.*, 268, 11492-5. ↗
- Schnapp, LM., Ramos, DM., Klimanskaya, IV., Pytela, R., Hatch, N., Sheppard, D. (1995). The human integrin alpha 8 beta 1 functions as a receptor for tenascin, fibronectin, and vitronectin. *J Biol Chem*, 270, 23196-202. ↗
- Horton, MA. (1997). The alpha v beta 3 integrin "vitronectin receptor". *Int J Biochem Cell Biol*, 29, 721-5. ↗
- Pytela, R., Sheppard, D., Nishimura, SL. (1994). Integrin alpha v beta 8. Interaction with vitronectin and functional divergence of the beta 8 cytoplasmic domain. *J Biol Chem*, 269, 28708-15. ↗
- McKeown-Longo, P., Memmo, LM. (1998). The alphavbeta5 integrin functions as an endocytic receptor for vitronectin. *J Cell Sci*, 111, 425-33. ↗

### Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.
2013-08-13	Revised	Jupe, S.

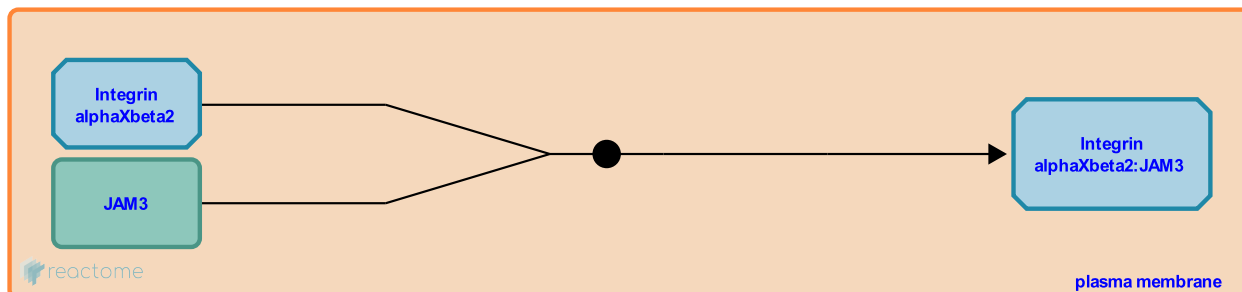
## Integrin alphaXbeta2 binds JAM3 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-202704

**Type:** binding

**Compartments:** plasma membrane



Although JAM-C is better known for its interaction with MAC-1, an interaction with CD11c/CD18 (known as alpha X beta 2), has also been described.

### Literature references

Linder, M., Ruf, A., Kroll, H., Santoso, S., Preissner, KT., Chavakis, T. et al. (2002). The junctional adhesion molecule 3 (JAM-3) on human platelets is a counterreceptor for the leukocyte integrin Mac-1. *J Exp Med*, 196, 679-91. ↗

Imhof, BA., Rainger, GE., Aurrand-Lions, M., Luscinskas, FW., Nourshargh, S., Ody, C. et al. (2007). JAM-C regulates unidirectional monocyte transendothelial migration in inflammation. *Blood*, 110, 2545-55. ↗

Weber, C., Fraemohs, L., Dejana, E. (2007). The role of junctional adhesion molecules in vascular inflammation. *Nat Rev Immunol*, 7, 467-77. ↗

### Editions

2007-11-12	Authored	Ouwehand, WH.
2007-11-12	Reviewed	Zwaginga, JJ.



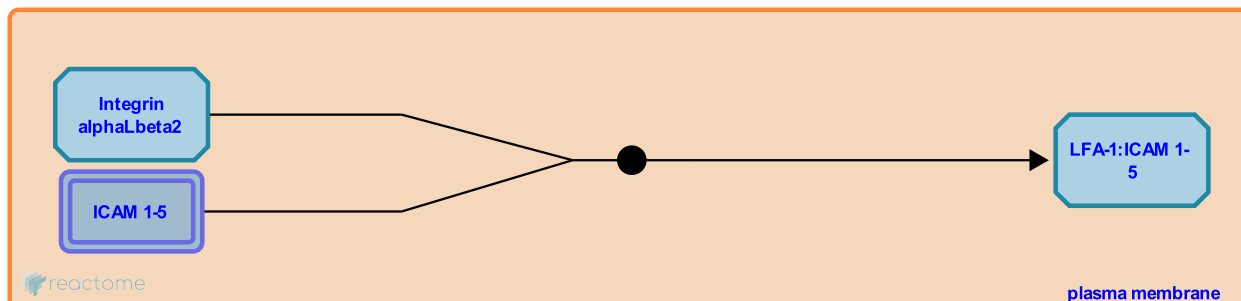
## ICAM1-5 bind Integrin alphaLbeta2 (LFA-1) ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-199050

**Type:** binding

**Compartments:** plasma membrane



Integrins play a central role in mediating lymphocyte adhesion to a number of surfaces. Integrin alphaLbeta2 (LFA-1) interacts with Inter cellular adhesion molecule (ICAM)1-5, which are typically expressed on other immune system cells. ICAM4 and 5 are known to be expressed on telencephalic neurons. VCAM-1 regulates lymphocyte adhesion to activated endothelial cells via Very Late Antigen-4 (VLA-4). To function in a circulating mode, leukocytes express LFA-1 and VLA-4 in a low ligand binding capacity. When leukocytes reach sites of inflammation, these integrins are switched to a higher binding state to guide the complex process of transmigration, tethering, rolling, arrest, adhesion and shape change. Signal cascades between LFA-1 and VLA-4 may cross-talk affecting binding affinities in a reciprocal fashion.

### Literature references

- Mori, K., Kagamiyama, H., Yoshihara, Y., Inazawa, J., Mizuno, T. (1997). cDNA cloning and chromosomal localization of the human telencephalin and its distinctive interaction with lymphocyte function-associated antigen-1. *J. Biol. Chem.*, 272, 1156-63. ↗
- Yusuf-Makagiansar, H., Murray, JS., Siahaan, TJ., Anderson, ME., Yakovleva, TV. (2002). Inhibition of LFA-1/ICAM-1 and VLA-4/VCAM-1 as a therapeutic approach to inflammation and autoimmune diseases. *Med Res Rev*, 22, 146-67. ↗

### Editions

2007-07-08	Authored	de Bono, B.
2007-08-06	Reviewed	Trowsdale, J.
2015-05-13	Reviewed	Barrow, AD.

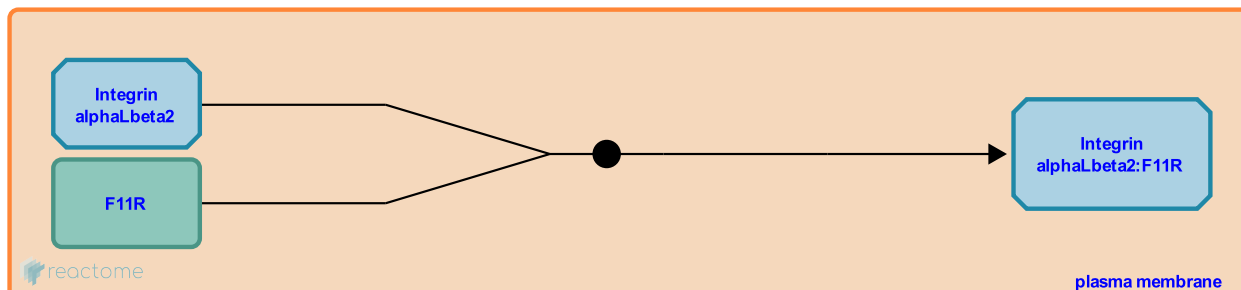
## Integrin alphaLbeta2 (LFA-1) binds F11R (JAM-A) ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-202718

**Type:** binding

**Compartments:** plasma membrane



JAM-A plays a key role in leukocyte transmigration and inflammatory extravasation. Transmigration of human leukocytes has been shown to involve heterophilic interactions of JAM-A with its integrin receptor LFA-1.

### Literature references

- Liehn, EA., Weber, C., Fraemohs, L., Lietz, M., Baltus, T., Zernecke, A. et al. (2005). Involvement of JAM-A in mononuclear cell recruitment on inflamed or atherosclerotic endothelium: inhibition by soluble JAM-A. *Arterioscler Thromb Vasc Biol*, 25, 729-35. ↗
- Weber, C., Fraemohs, L., Koenen, RR., Heinemann, B., Ostermann, G. (2004). The functional interaction of the beta 2 integrin lymphocyte function-associated antigen-1 with junctional adhesion molecule-A is mediated by the I domain. *J Immunol*, 173, 6259-64. ↗
- Weber, C., Weber, KS., Zernecke, A., Ostermann, G., Schroder, A. (2002). JAM-1 is a ligand of the beta(2) integrin LFA-1 involved in transendothelial migration of leukocytes. *Nat Immunol*, 3, 151-8. ↗
- Weber, C., Fraemohs, L., Dejana, E. (2007). The role of junctional adhesion molecules in vascular inflammation. *Nat Rev Immunol*, 7, 467-77. ↗

### Editions

2007-11-12	Authored	Ouwehand, WH.
2007-11-12	Reviewed	Zwaginga, JJ.

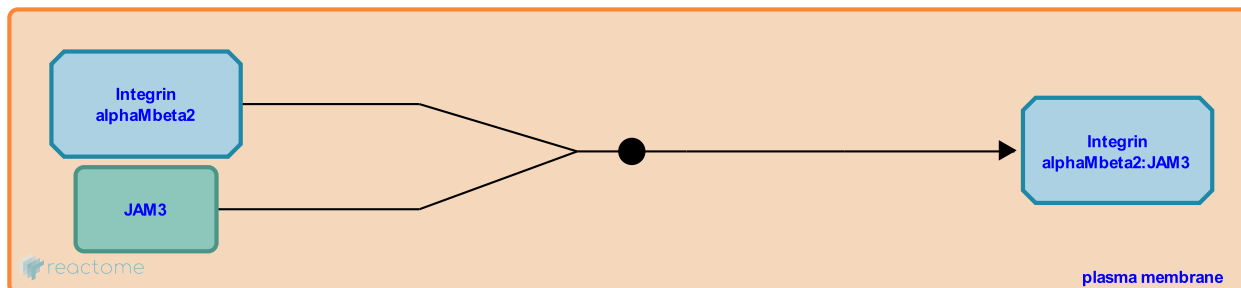
## Integrin alphaMbeta2 (MAC1) binds JAM3 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-202727

**Type:** binding

**Compartments:** plasma membrane



Recruitment of monocytic cells to the vessel wall by platelets is mediated via CD11b/CD18 (Mac-1) and platelet JAM-C. In the case of dendritic cells, this interaction leads to their activation and platelet phagocytosis. This process may be of importance for progression of atherosclerotic lesions.

### Literature references

Stellos, K., Wesselborg, S., Santoso, S., Seizer, P., Wendel, HP., May, AE. et al. (2007). Platelets recruit human dendritic cells via Mac-1/JAM-C interaction and modulate dendritic cell function in vitro. *Arterioscler Thromb Vasc Biol*, 27, 1463-70. ↗

Weber, C., Fraemohs, L., Dejana, E. (2007). The role of junctional adhesion molecules in vascular inflammation. *Nat Rev Immunol*, 7, 467-77. ↗

### Editions

2007-11-12	Authored	Ouwehand, WH.
2007-11-12	Reviewed	Zwaginga, JJ.

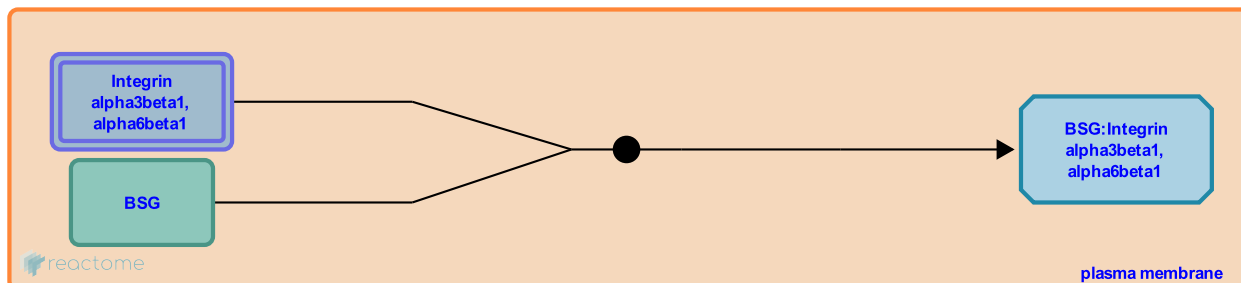
## BSG (basigin) binds Integrin alpha3beta1, alpha6beta1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-204434

**Type:** binding

**Compartments:** plasma membrane



Basigin is a widely distributed cell-surface protein with two immunoglobulin domains and has shown to associate with both the integrins alpha3beta1 and alpha6beta1.

### Literature references

Bodorova, J., Hemler, ME., Berditchevski, F., Chang, S. (1997). Generation of monoclonal antibodies to integrin-associated proteins. Evidence that alpha3beta1 complexes with EMMPRIN/basigin/OX47/M6. *J Biol Chem*, 272, 29174-80. ↗

### Editions

2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

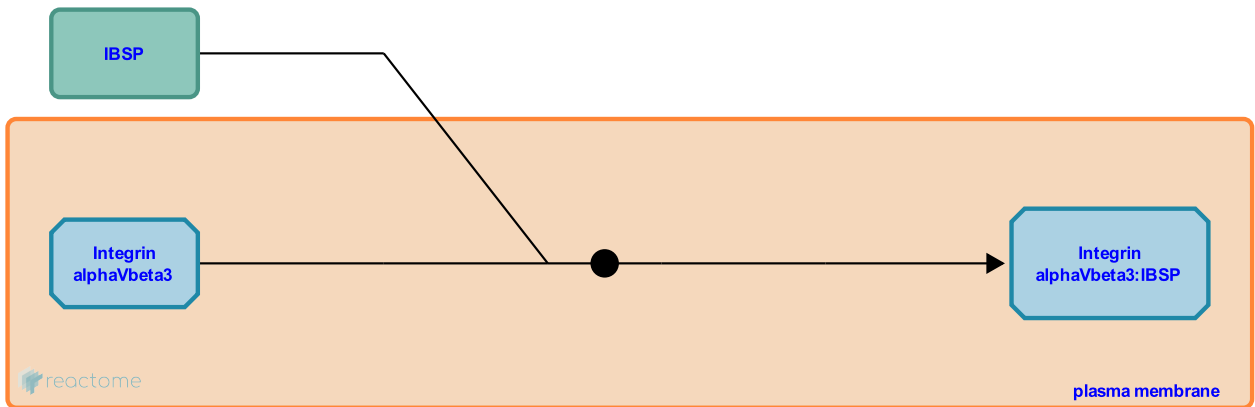
# Interaction of integrin alphaVbeta3 with IPSP (Bone sialoprotein 2) ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-265427

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Integrin alphaVbeta3 receptor has been implicated in various physiological and pathological responses, including bone density, angiogenesis, apoptosis, tumor growth and metastasis.

Bone sialoprotein (BSP) is a significant component of the bone extracellular matrix and plays an important role in bone resorption and osteoclast formation. BSP is considered as an important physiological ligand of alphaVbeta3 for osteoclast adhesion in bone development and mineralization.

## Literature references

Midura, RJ., Kim, W., Plow, EF., Byzova, TV. (2000). Activation of integrin alpha(V)beta(3) regulates cell adhesion and migration to bone sialoprotein. *Exp Cell Res*, 254, 299-308. ↗

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

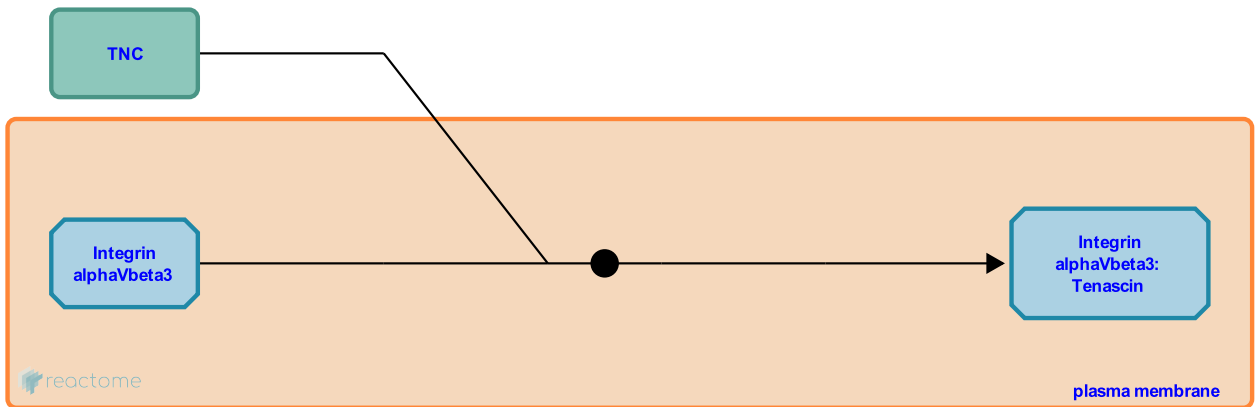
# Interaction of integrin alphaVbeta3 with Tenascin [↗](#)

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-265426

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Tenascin, an extracellular matrix protein acts as a ligand to multiple integrin receptors including alphaVbeta3. Integrin alphaVbeta3 binds to the third fibronectin type III repeat in tenascin (Tnfn3) and induces the cell proliferation.

## Literature references

Monis, H., Yokosaki, Y., Sheppard, D., Chen, J. (1996). Differential effects of the integrins alpha9beta1, alphavbeta3, and alphavbeta6 on cell proliferative responses to tenascin. Roles of the beta subunit extracellular and cytoplasmic domains. *J Biol Chem*, 271, 24144-50. [↗](#)

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

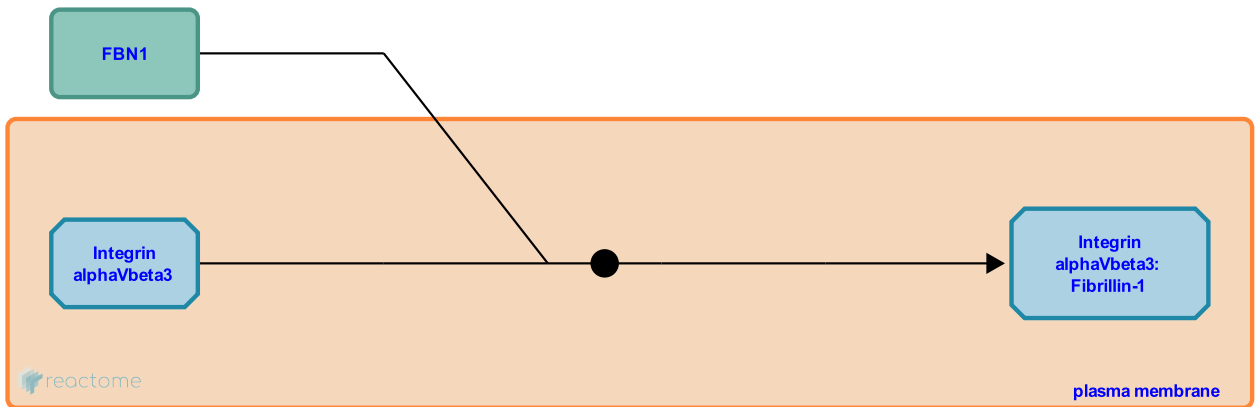
# Interaction of integrin alphaVbeta3 with Fibrillin [↗](#)

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-265423

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Fibrillins are the main constituents of the extracellular microfibrils that form a template for tropoelastin during elastic fibrillogenesis. Fibrillins polymerize extracellularly as parallel bundles of head-to-tail monomers. The integrin receptor alphaVbeta3 is the major receptor for the fibrillin ligands and influences cell shape and migration, focal complex formation, signaling and ECM deposition.

## Literature references

Humphries, MJ., Lomas, A., Kielty, CM., Humphries, J., Shuttleworth, CA., Bax, DV. et al. (2003). Cell adhesion to fibrillin-1 molecules and microfibrils is mediated by alpha 5 beta 1 and alpha v beta 3 integrins. *J Biol Chem*, 278, 34605-16. [↗](#)

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

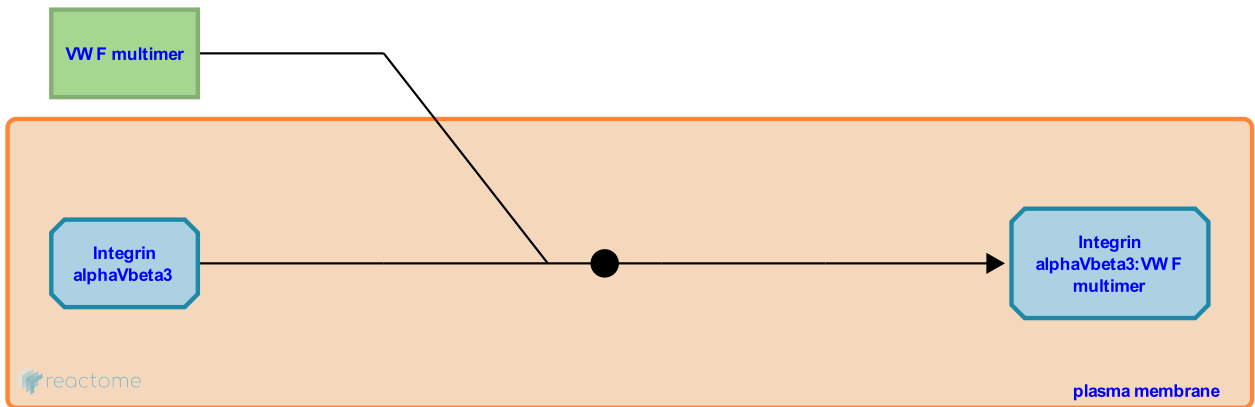
# Interaction of integrin alphaVbeta3 with von Willbrand Factor ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-265425

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Integrin alphaVbeta3 interacts with von Willebrand factor (vWF) on the RGD motif (1744-1746 residues) present on the mature vWF subunit.

## Literature references

Lu, X., Denis, C., Meyer, D., Baruch, D., Williams, JA. (1993). Solid-phase von Willebrand factor contains a conformationally active RGD motif that mediates endothelial cell adhesion through the alpha v beta 3 receptor. *Blood*, 82, 3622-30. ↗

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.



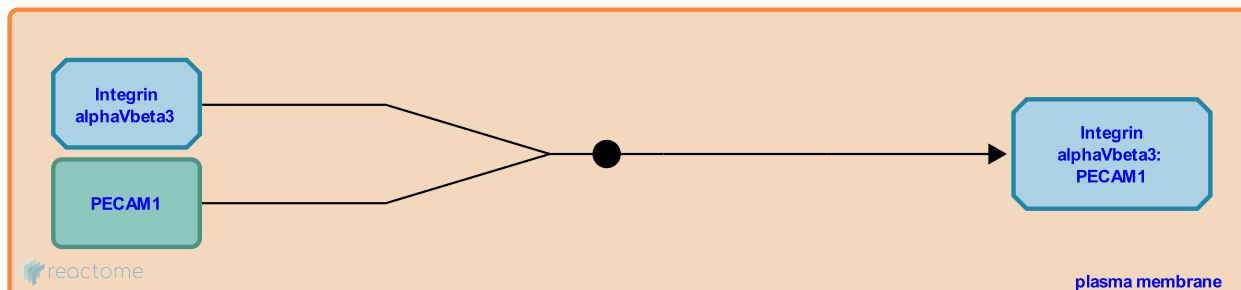
## Interaction of integrin alphaVbeta3 with PECAM1 [↗](#)

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-210304

**Type:** binding

**Compartments:** plasma membrane



Alpha v beta 3 integrin is one of the potential heterophilic ligands of PECAM-1 that is involved in down-regulation of T-cell responses. The heterophilic interaction of alpha v beta 3 integrin on endothelial cells with PEACAM-1 on leukocytes increases the adhesive function of beta integrins on T cells, monocytes, neutrophils and NK cells suggesting that leukocyte PEACAM-1 act as a signaling molecule.

### Literature references

Imhof, BA., Bachmann, F., Piali, L., Uhrek, C., Dunon, D., Gisler, RH. et al. (1995). CD31/PECAM-1 is a ligand for alpha v beta 3 integrin involved in adhesion of leukocytes to endothelium. *J Cell Biol*, 130, 451-60. [↗](#)

Buckley, CD., Brown, EJ., Simmons, DL., Blystone, SD., Newton, JP., Doyonnas, R. et al. (1996). Identification of alpha v beta 3 as a heterotypic ligand for CD31/PECAM-1. *J Cell Sci*, 109, 437-45. [↗](#)

### Editions

2008-02-26	Authored	de Bono, B., Garapati, P V.
2008-02-26	Reviewed	Trowsdale, J.

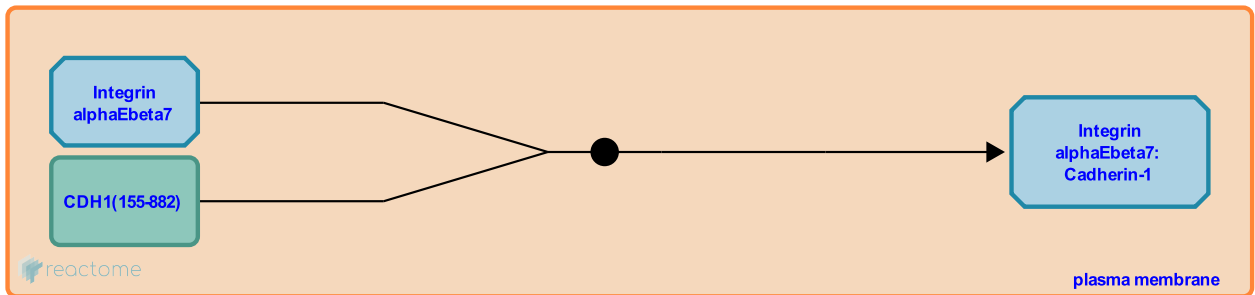
# Interaction of integrin alphaEbeta7 with Cadherin-1 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-265422

**Type:** binding

**Compartments:** plasma membrane



E-cadherin, member of the cadherin superfamily is a calcium-dependent cell adhesion protein expressed on the epithelial cells. The integrin alphaEbeta7 is selectively expressed on intestinal intraepithelial T lymphocytes and CD8+ T lymphocytes in inflammatory lesions near epithelial cells. E-cadherin undergoes both homophilic and heterophilic interactions. It is the only binding partner for alphaEbeta7. This interaction plays a key role in the proliferation of intrathymic T cell populations, T lymphocyte development and damage of target epithelia.

## Literature references

Petrie, HT., Prockop, SE. (2004). Functional assessment of alphaEbeta7/E-cadherin interactions in the steady state postnatal thymus. *Clin Dev Immunol*, 11, 135-41. ↗

Tsuzaka, K., Abe, T., Nozaki, K., Yoshimoto, K., Kumazawa, C., Tsubota, K. et al. (2005). Critical role of the fifth domain of E-cadherin for heterophilic adhesion with alpha E beta 7, but not for homophilic adhesion. *J Immunol*, 175, 1014-21. ↗

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2008-03-11	Edited	Garapati, P V.
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2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

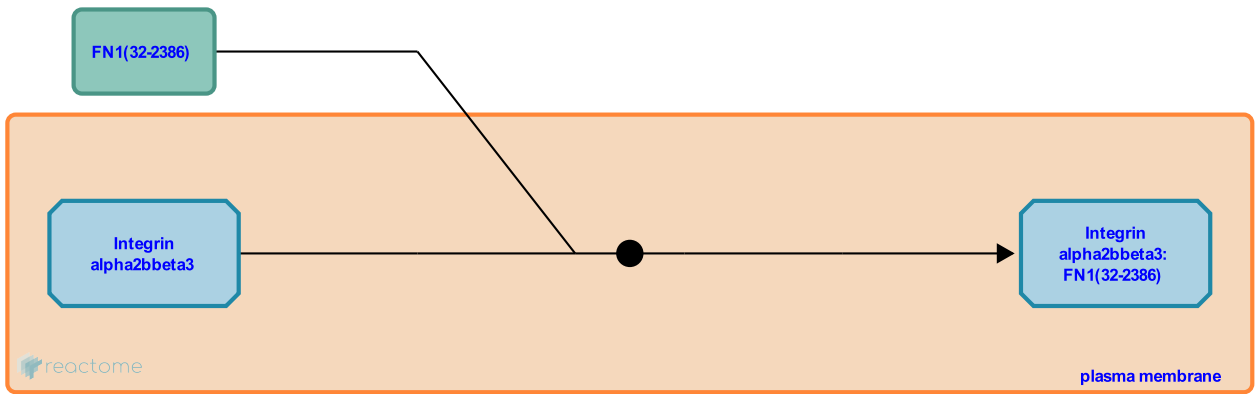
# Interaction of integrin alphaIIb beta3 with Fibronectin ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-349593

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Fibronectin plays a role in cell adhesion and cell migration. It mediates platelet adhesion in the vasculature by interacting with integrin alphaIIb beta3.

## Literature references

Mather, T., Nollert, MU., Chada, D. (2006). The synergy site of fibronectin is required for strong interaction with the platelet integrin alphaIIb beta3. *Ann Biomed Eng*, 34, 1542-52. ↗

## Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

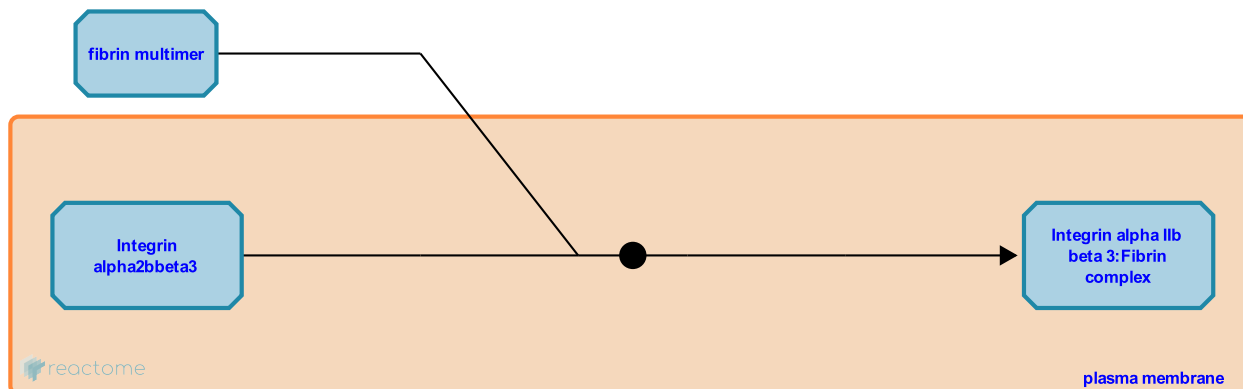
## Adhesion of integrin alphaIIb beta3 to fibrin network ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-114560

**Type:** binding

**Compartments:** plasma membrane, extracellular region



At the beginning of this reaction, 1 molecule of 'fibrin multimer', and 1 molecule of 'Alpha IIb Beta 3 Integrin' are present. At the end of this reaction, 1 molecule of 'Integrin alpha IIb beta 3:Fibrin complex' is present.

## Literature references

Shattil, SJ. (1999). Signaling through platelet integrin alpha IIb beta 3: inside-out, outside-in, and sideways. *Thromb Haemost*, 82, 318-25. ↗

## Editions

2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

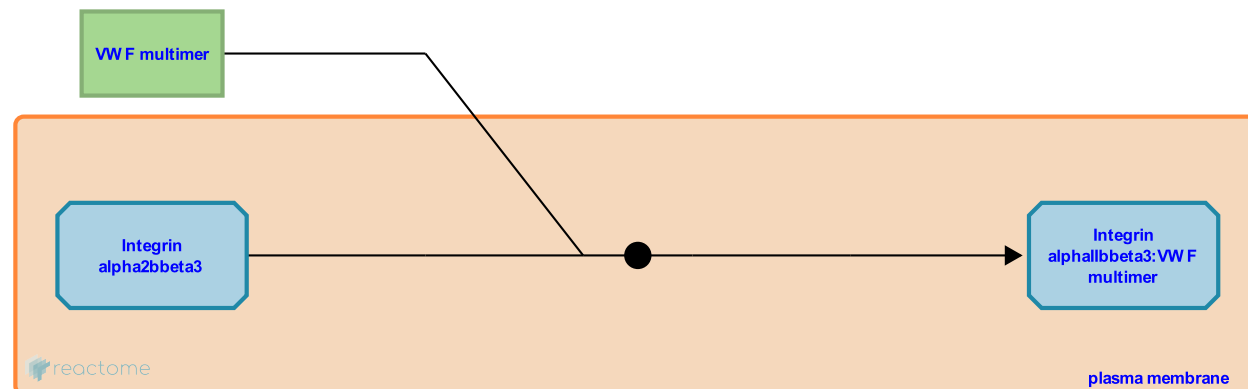
## Interaction of integrin alphaIIb beta3 with von Willebrand factor ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-216072

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Integrin alphaIIb beta3 (glycoprotein IIb-IIIa, GP IIb-IIIa) is one of the major platelet receptor that is involved in aggregation and adhesion of platelets. In resting stage alphaIIb beta3 is inactive and does not interact with its ligands but upon activation or vascular injury it binds to the ECM protein von Willebrand factor (vWf) and stimulate the platelet aggregation.

### Literature references

Giuliano, S., Jackson, SP., Rooney, M., Nesbitt, WS. (2003). Bidirectional integrin alphaIIb beta3 signalling regulating platelet adhesion under flow: contribution of protein kinase C. *Biochem J*, 372, 163-72. ↗

Harper, IS., Yap, CL., Goncalves, I., Giuliano, S., Kulkarni, S., Jackson, SP. et al. (2002). Distinct glycoprotein Ib/V/IX and integrin alpha IIb beta 3-dependent calcium signals cooperatively regulate platelet adhesion under flow. *J Biol Chem*, 277, 2965-72. ↗

### Editions

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

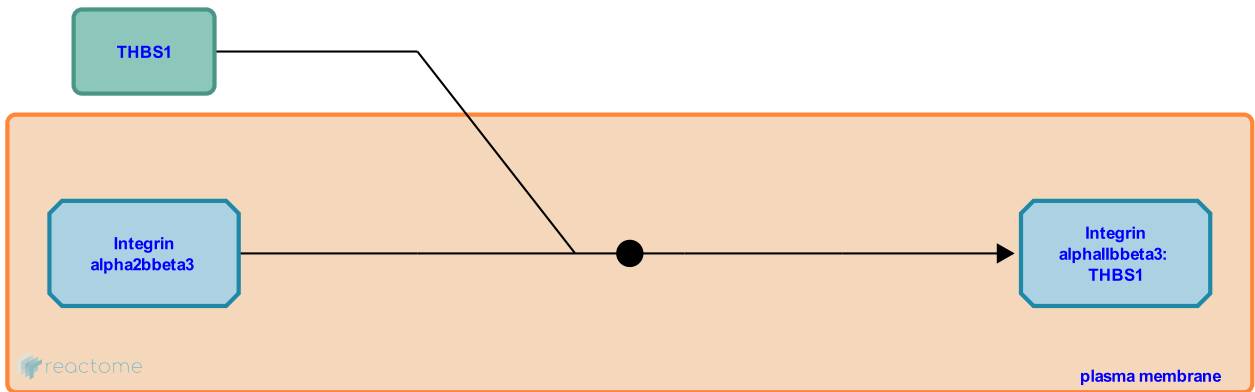
**Interaction of integrin alphaIIb beta 3 with THBS1 (Thrombospondin-1)** ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-349603

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Thrombospondin-1 (TSP-1) secreted from platelet alpha granules on thrombin activation associates with actin cytoskeleton. This association of TSP-1 with actin cytoskeleton is mediated by the membrane receptor alphaIIb beta3.

**Literature references**

Tuszynski, GP., Kowalska, MA. (1991). Thrombospondin-induced adhesion of human platelets. *J Clin Invest*, 87, 1387-94. ↗

**Editions**

2008-03-11	Edited	Garapati, P V.
2008-05-07	Authored	Geiger, B., Horwitz, AR.
2008-05-07	Reviewed	Humphries, MJ., Yamada, KM., Hynes, R.

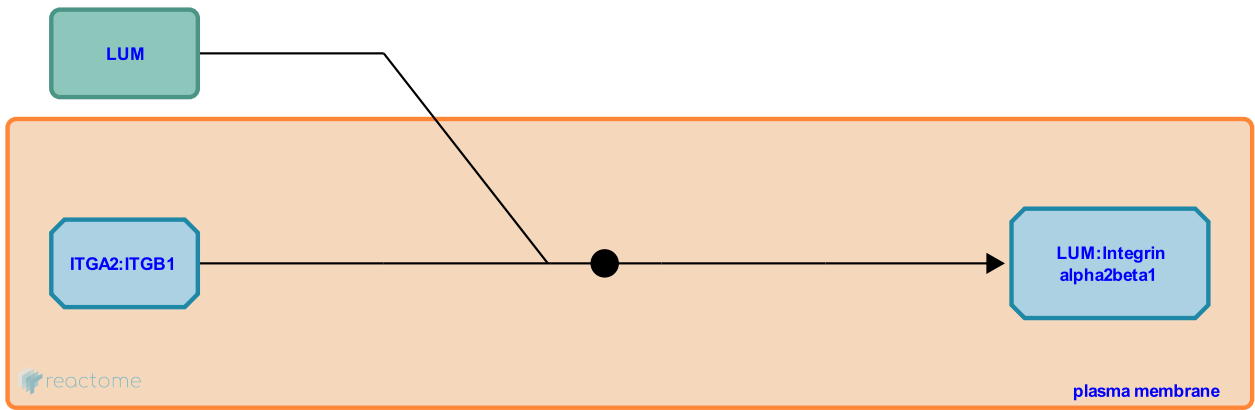
**LUM (lumican) binds integrin alpha2beta1** [↗](#)

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4085133

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Lumican (LUM) is the major leucine-rich keratan sulfate proteoglycan of the corneal stroma, also found in the extracellular matrices of skin, muscle and cartilage. Lum null mice have corneal opacity as well as skin and tendon fragility associated with disorganized and loosely packed collagen fibers (Jepsen et al. 2002, Chakravarti et al. 2003). LUM binds integrin alpha2beta1 (Zeltz et al. 2010), downregulating MMP-14 expression (Niewiarowska et al. 2011).

**Literature references**

Wegrowski, Y., Eble, JA., Brezillon, S., Perreau, C., Zeltz, C., Heino, J. et al. (2010). Lumican inhibits cell migration through  $\alpha 2 \beta 1$  integrin. *Exp. Cell Res.*, 316, 2922-31. [↗](#)

**Editions**

2012-08-08	Authored	Jupe, S.
2013-08-13	Edited	Jupe, S.
2013-08-13	Reviewed	Ricard-Blum, S.

## AGRN binds Integrins alphaVbeta1 (Other beta1-containing integrins) ↗

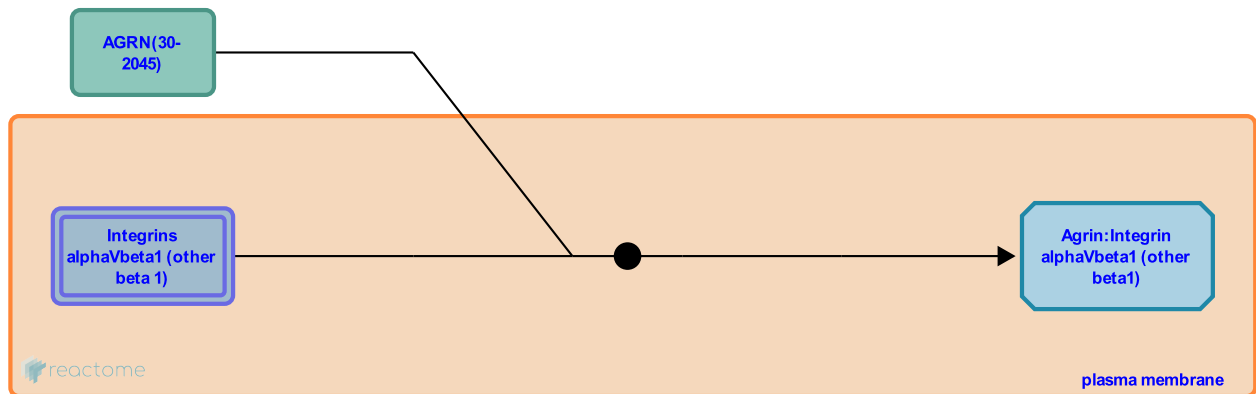
**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-2467436

**Type:** binding

**Compartments:** plasma membrane, extracellular region

**Inferred from:** [Agrin binds Integrin alphaVbeta1 \(alpha1beta1\) \(Gallus gallus\)](#)



Agrin (AGRN) is a >400 kDa multi-domain heparan sulfate proteoglycan found in basement membranes. It is a critical organizer of postsynaptic differentiation at the skeletal neuromuscular junction; synaptogenesis is profoundly disrupted in its absence (Gautam et al. 1996). Two alternate N-termini exist. The predominant longer LN form (Burgess et al. 2000) starts with a secretion signal sequence and a laminin-binding domain (Denzer et al. 1995, Kammerer et al. 1999); the shorter SN form associates with the plasma membrane (Burgess et al. 2000, Neumann et al. 2001). Following the SN or LN regions are 8 follistatin repeats, known to bind growth factors and inhibit proteases in other proteins. The central region has two repeats homologous to domain III of laminin. The C-terminal portion, which is responsible for the molecule's known signaling functions, contains four EGF repeats and three LG (G) domains homologous to those found in laminin alpha chains, neurexins and slits (Timpl et al. 2000).

The LG domains bind alphaVbeta1 and another beta1-containing integrin (Martin & Sanes 1997, Burgess et al. 2002, Bezakova & Ruegg 2003). The N-terminus of the LN form of AGRN binds to the laminin gamma-1 subunit (Denzer et al. 1997, Kammerer et al. 1999). This may indirectly bind AGRN to integrins on the cell surface (Bezakova & Ruegg 2003).

### Editions

2012-08-08	Authored	Jupe, S.
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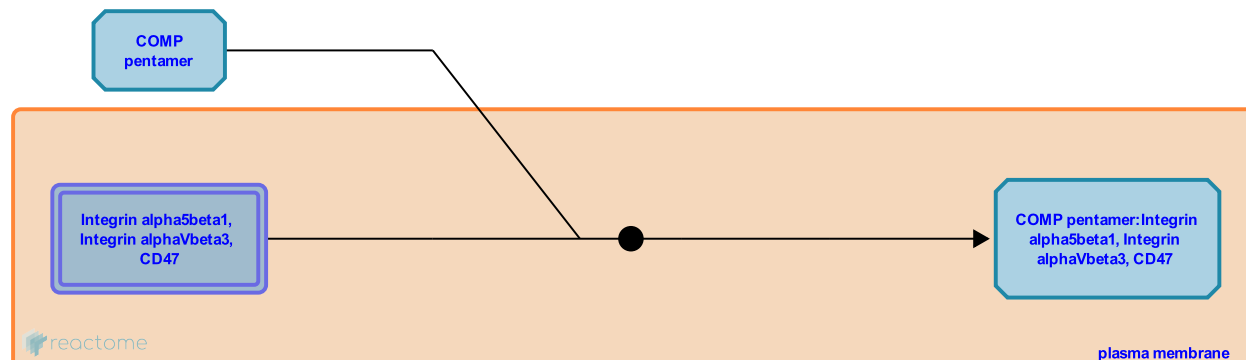
## COMP binds Integrin alpha5beta1, Integrin alphaVbeta3, CD47 ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-2426259

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Cartilage oligomeric matrix protein (COMP, thrombospondin-5) is a 524-kDa pentameric glycoprotein expressed primarily in cartilage, tendon, ligament and synovium. In adult cartilage, COMP has been shown to be located primarily in the inter-territorial matrix between chondrocytes (Murphy et al. 1999). The mature protein is pentameric with each monomer linked to its neighbour by a disulphide bond, located at the amino terminus of the protein (Hedbom et al. 1992, Morgelin et al. 1992).

COMP binds integrin alpha5beta1 (Chen et al. 2005), integrin alphaVbeta3 (Neidhart et al. 2005) and CD47 (also known as integrin-associated peptide or IAP, Rock et al. 2010) on the cell surface of chondrocytes and fibroblasts.

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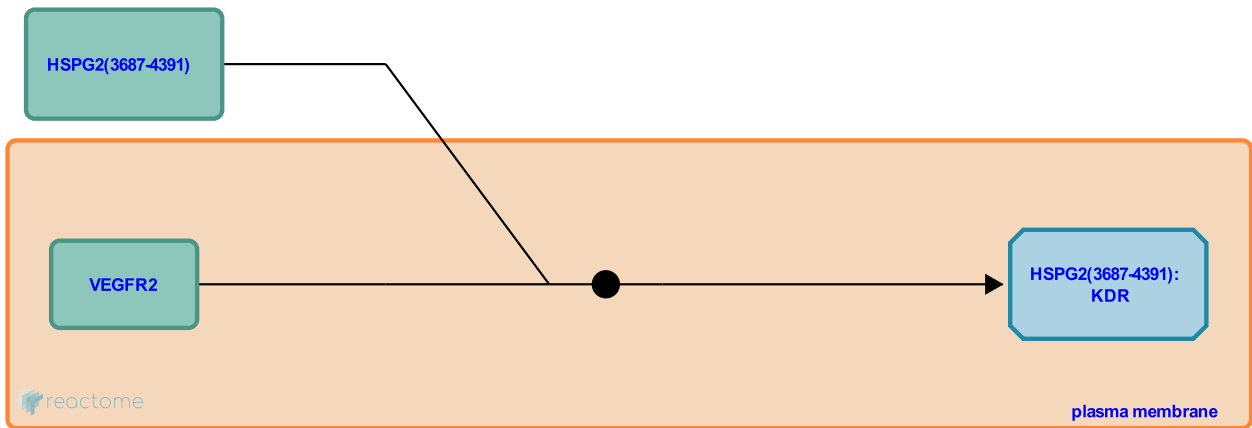
# Endorepellin binds KDR (VEGFR2) ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4088281

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Endorepellin is the C-terminal domain V of perlecan, constituting amino acids 3687–4391 (Mongiat et al. 2004). It has anti-angiogenic properties, blocking endothelial cell adhesion to fibronectin and type I collagen (Mongiat et al. 2003). Endorepellin and a smaller fragement constituting the third laminin G–like (LG) domain (LG3) disrupt actin stress fibers and focal adhesions via an interaction with the collagen receptor alpha2beta1 integrin (Bix et al. 2004). The first and second laminin G domains 1 of endorepellin bind specifically and with high affinity to Ig domains 3–5 of VEGFR2 (Willis et al. 2013).

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Iozzo, RV., Mongiat, M., Poluzzi, C., Willis, CD. (2013). Endorepellin laminin-like globular 1/2 domains bind Ig3-5 of vascular endothelial growth factor (VEGF) receptor 2 and block pro-angiogenic signaling by VEGFA in endothelial cells. *FEBS J.*, 280, 2271-84. ↗

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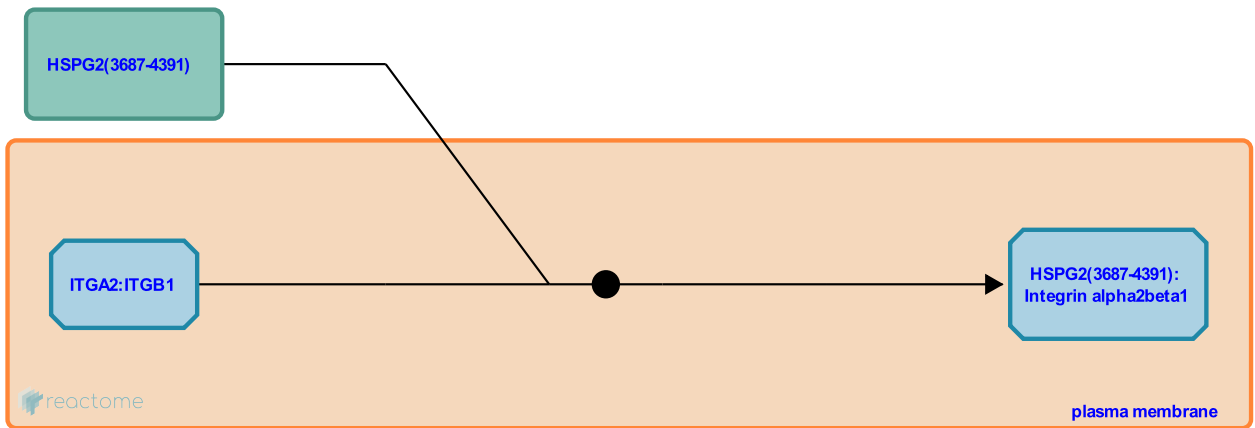
# Endorepellin binds alpha2beta1 integrin ↗

**Location:** [Integrin cell surface interactions](#)

**Stable identifier:** R-HSA-4088220

**Type:** binding

**Compartments:** plasma membrane, extracellular region



Endorepellin is the C-terminal domain V of perlecan, constituting amino acids 3687–4391 (Mongiat et al. 2004). It has anti-angiogenic properties, blocking endothelial cell adhesion to fibronectin and type I collagen (Mongiat et al. 2003). Endorepellin and a smaller fragement constituting the third laminin G–like (LG) domain (LG3) disrupts actin stress fibers and focal adhesions via an interaction with the collagen receptor alpha2beta1 integrin (Bix et al. 2004). Laminin G domains 1 and 2 of endorepellin bind specifically and with high affinity to Ig domains 3–5 of VEGFR2 (Willis et al. 2013).

## Literature references

Kim, JK., Zutter, MM., Macro, L., Iozzo, RV., Bix, G., Santoro, SA. et al. (2004). Endorepellin causes endothelial cell disassembly of actin cytoskeleton and focal adhesions through alpha2beta1 integrin. *J. Cell Biol.*, 166, 97-109. ↗

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# Table of Contents

Introduction	1
 Integrin cell surface interactions	2
 Collagen types III, IV, V, VI, VIII, IX, XVI bind integrins alpha1beta1 and alpha2beta1	3
 Collagen type I binds integrin alpha1beta1, alpha2beta1, alpha10beta1	5
 Collagen type I binds integrin alpha11beta1	6
 Collagen type II binds integrin alpha2beta1, alpha1beta1, alpha11beta1	7
 Collagen type II binds integrin alpha10beta1	8
 Collagen type IV networks bind integrins alpha1beta1, alpha2beta1	9
 Collagen type VII binds integrin alpha2beta1	10
 Collagen type X binds Integrin alpha2beta1	11
 Collagen type XIII binds Integrin alpha1beta1	12
 Collagen type XXIII binds Integrin alpha2beta1	13
 Collagen types VI, IX bind integrin alpha10beta1	14
 Collagen type IV binds integrin alpha10beta1	15
 Collagen type IX binds integrin alpha11beta1	16
 Arresten binds integrin alpha1beta1	17
 Endostatin binds integrin alphaVbeta3, alphaVbeta5, alpha3beta1, alpha5beta1	18
 Tumstatin binds integrin alphaVbeta 3, alpha3beta1	19
 Canstatin binds integrins alphaVbeta3, alphaVbeta5	20
 Tetrastatin binds integrin alphaVbeta3	21
 THBS1 (Thrombospondin-1) binds Integrin alpha3beta1, alpha4beta1	22
 Integrins alpha4beta1, alpha8beta1, alphaVbeta1, alphaVbeta3, alphaVbeta6 bind Fibronectin matrix	23
 SPP1 (osteopontin) binds integrin alpha5beta1, alpha9beta1	24
 SPP1 (osteopontin) binds Integrin alpha4beta1	25
 SPP1 (osteopontin) binds integrin alpha8beta1	26
 SPP1 (osteopontin) binds integrins alphaVbeta1, alphaVbeta3, alphaVbeta5	27
 SPP1 (osteopontin) binds CD44	28
 VCAM1 binds Integrin alpha4beta1	29
 Integrin alpha4beta1 binds JAM2:JAM3	30
 ITGA4:ITGB1 binds natalizumab	31
 MADCAM1-1 binds Integrin alpha4beta7	32
 Interaction of integrin alpha8beta1 with Tenascin-C	33
 Interaction of integrin alpha9beta1 with VCAM1	34
 Interaction of integrin alpha9beta1 with Tenascin-C	35

↗ Interaction of integrin alphaDbeta2 with fibrin	36
↗ Interaction of integrin alphaXbeta2 with fibrin	37
↗ VTN (vitronectin) binds Integrin alphaVbeta3, alphaVbeta5, alphaVbeta8	38
↗ Integrin alphaXbeta2 binds JAM3	39
↗ ICAM1-5 bind Integrin alphaLbeta2 (LFA-1)	40
↗ Integrin alphaLbeta2 (LFA-1) binds F11R (JAM-A)	41
↗ Integrin alphaMbeta2 (MAC1) binds JAM3	42
↗ BSG (basigin) binds Integrin alpha3beta1, alpha6beta1	43
↗ Interaction of integrin alphaVbeta3 with IPSP (Bone sialoprotein 2)	44
↗ Interaction of integrin alphaVbeta3 with Tenascin	45
↗ Interaction of integrin alphaVbeta3 with Fibrillin	46
↗ Interaction of integrin alphaVbeta3 with von Willbrand Factor	47
↗ Interaction of integrin alphaVbeta3 with PECAM1	48
↗ Interaction of integrin alphaEbata7 with Cadherin-1	49
↗ Interaction of integrin alphaIIbbeta3 with Fibronectin	50
↗ Adhesion of integrin alphaIIbbeta3 to fibrin network	51
↗ Interaction of integrin alphaIIbbeta3 with von Willebrand factor	52
↗ Interaction of integrin alphaIIb beta 3 with THBS1 (Thrombospondin-1)	53
↗ LUM (lumican) binds integrin alpha2beta1	54
↗ AGRN binds Integrins alphaVbeta1 (Other beta1-containing integrins)	55
↗ COMP binds Integrin alpha5beta1, Integrin alphaVbeta3, CD47	56
↗ Endorepellin binds KDR (VEGFR2)	57
↗ Endorepellin binds alpha2beta1 integrin	58
Table of Contents	59