An $\alpha_1/\beta_1$-like Integrin Receptor on Rat Aortic Smooth Muscle Cells Mediates Adhesion to Laminin and Collagen Types I and IV

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Extracellular matrix receptors on vascular smooth muscle cells may enable the cells to migrate through both interstitial and basement membrane matrices during vascular remodelling after injury. Rat aortic smooth muscle cells attach to surfaces coated with fibronectin, laminin, and collagen types I and IV. Members of the $\beta$ family of integrin receptors appear to mediate attachment to these extracellular matrix components. We used a monoclonal antibody, 3A3, to identify a 185/120 kD, $\alpha_1/\beta_1$-like, heterodimeric integrin receptor that mediates rat aortic smooth muscle cell adhesion to collagen types I and IV as well as to laminin. This receptor appears to be the only $\beta$ integrin receptor mediating adhesion to type IV collagen. On the other hand, the smooth muscle cells have several other $\beta$ integrin receptors in addition to the 185/120 kD receptor that bind to laminin- and to collagen type I-Sepharose affinity columns. By using 3A3 to inhibit only the 185/120 kD receptor, we suggest that these other receptors also can be used by rat aortic smooth muscle cells to attach to laminin and collagen type I. (Arteriosclerosis 10:402–409, May/June 1990)

During atherosclerosis, smooth muscle cells residing in the aortic media migrate into the intima and undergo a phenotypic change from a contractile to a synthetic state. Associated with this change in phenotypic state, there is an increased production of extracellular matrix (ECM) components, as well as a change in the type of ECM components that surround the smooth muscle cells. For example, synthetic state smooth muscle cells have only a disrupted, incomplete basement membrane, whereas smooth muscle cells in the contractile state are surrounded by a distinct basement membrane. Compared with cells in the contractile state, cells in a synthetic state have an increased secretion of fibronectin, elastin, glycosaminoglycans, and collagen types I, IV, V, and VI.

It is known that the adhesive properties of the substratum may influence the shape of cells and thereby modify their synthesis of proteins, RNA, and DNA, as well as their response to hormones and growth factors. ECM proteins have been shown not only to promote smooth muscle cell adhesion and migration but also to influence the phenotypic appearance of smooth muscle cells.

The response of the smooth muscle cell to the ECM probably depends on specific cell surface receptors. In vivo, aortic smooth muscle cells form dense adhesion plaques at the junction between the ECM and the intracellular contractile microfilament system. A group of related cell-surface glycoproteins, called integrins, have been implicated as surface receptors for mediating adhesion to the ECM and to other cells. Each receptor is a heterodimer in which one of several homologous $\alpha$ subunits associates noncovalently with a $\beta$ subunit. The integrins require the presence of divalent cations to function. In human cells, there are at least five subfamilies of integrin receptors, which are defined by their component $\beta$ chains. The first subfamily comprises at least seven related complexes, each consisting of a $\beta$ chain with a distinct companion $\alpha$ chain. Members of the $\beta$ subfamily include receptors for fibronectin ($\alpha_5\beta_1$ and $\alpha_5\beta_3$), laminin ($\alpha_{3\beta_1}$, $\alpha_{5\beta_1}$, $\alpha_{6\beta_1}$, and $\alpha_{2\beta_1}$), and collagen types I and IV ($\alpha_{1\beta_1}$, $\alpha_{2\beta_1}$, and $\alpha_{3\beta_1}$).

Rat aortic smooth muscle (RASM) cells attach to dishes coated with ECM proteins (laminin, fibronectin, and collagen types I and IV (R.I. Clyman et al., unpublished observations). Cell attachment to these substrates appears to be mediated by members of the $\beta$ family of ECM receptors. The presence of divalent cations is necessary for RASM cell attachment to the ECM proteins, but not to other attachment proteins (poly-L-lysine or wheat germ agglutinin). Antibodies to the $\beta$ subunit not only show the presence of integrin complexes in focal adhesion plaques on each substrate but also block cell adhesion to the different substrates (R.I. Clyman et al., unpublished observations). A series of receptor complexes that are recognized by several antisera to the $\beta$ subunit has been isolated by ligand-affinity chromatography and sodium dodecyl sulfate-polyacrylamide gel elec-
Antibodies were generously supplied by Hynda Kleinman and George Martin (NIH), and the antibody to entactin was a generous gift of Kevin Tomaselli and Louis Reichardt (University of California, San Francisco). Heat-inactivated normal rabbit and goat sera or irrelevant mouse MABs were used as controls.

Cell Adhesion Assay

Cell adhesion was measured by using a previously described assay.29 Cells were labeled for 18 to 24 hours with 2 μCi/ml of 5-3H-iodo-2'-deoxyuridine (3H-IUdR, ICN, Costa Mesa, CA). Protein synthesis was inhibited by pre-incubating the cultures with cycloheximide (25 μg/ml) for 3 hours before cell harvest. Cycloheximide was included in the culture media used in the subsequent adhesion assay. The cells were removed from the culture plates by brief incubation (2 minutes) at room temperature with trypsin-EDTA; this method has been used previously in studying integrins.33,34 The trypsin was inactivated by washing the cells with DME plus 5% fetal bovine serum (FBS) at 4°C. The cell pellet was resuspended in DME plus 1 mg/ml of bovine serum albumin (BSA) for the assay.

The wells of uncharged polystyrene 96-well microtiter plates (Serocluster, Costar, Cambridge, MA) were pre-coated with 10 μg/ml of poly-L-lysine (Mr 500 000, Sigma); 10 μg/ml of wheat germ agglutinin (Calbiochem, San Diego, CA); 8.75 μg/ml of fibronectin; 20 μg/ml of laminin; 1 μg/ml of type IV collagen; and 5 μg/ml of type I collagen. Fibronectin was purified from outdated human plasma by using gelatin-Sepharose affinity chromatography.35 Collagen type I (>97%) from bovine skin was purchased from Collagen (Palo Alto, CA). Both laminin and collagen type IV were isolated by the protocol of Kleinman et al.36 from Engelbreth Holm Swarm tumors grown in C57BL/6 mice. The laminin used in these experiments was found to be free of type IV collagen and entactin both by an enzyme-linked immunosorbent assay and by immunoblotting, as previously described.37,38 The affinity-purified antibodies to laminin and type IV collagen were generously supplied by Hynda Kleinman and George Martin (NIH), and the antibody to entactin was a gift of Albert Chung (University of Pennsylvania). The concentration of substrate used to precoat the wells was the concentration that allowed 80% to 90% of the maximal RASM cell attachment to that particular substrate (R.I. Clyman et al., unpublished observations). The wells were then washed with PBS, and nonspecific adherence to the coated wells was blocked with 1 mg/ml BSA in DME for 1 hour at 37°C. Appropriate dilutions of antibodies were added to the wells. The 3H-labeled cells (2×10⁶ cells/well) were allowed to attach to the wells for 15 minutes at 37°C. We have previously found that 70% to 95% of maximal RASM cell attachment to a substrate occurred.
during that interval of incubation (R.I. Clyman et al., unpublished observations).

**Cell Surface Radiolodination**

For surface labeling, the cell monolayer was washed five times with Ca\(^{2+}\)/Mg\(^{2+}\)-free PBS before adding iodination buffer (50 mM Tris HCl, pH 7.4, 150 mM NaCl, 1 mM MnSO\(_4\), 20 mM glucose) to the culture dish. Iodination was initiated by adding glucose oxidase (Sigma), lactoperoxidase (Calbiochem), and carrier-free Na\(^{125}\)I (Amersham) at final concentrations of 200 mM/ml, 200 \(\mu\)g/ml, and 1 mg/ml, respectively. The culture dish was rocked for 10 minutes at room temperature; the reaction was terminated with excess glucose-free iodination buffer at 4°C. Membrane proteins were solubilized by extracting the radiolabeled cells for 1 hour with a 4°C solution of 200 mM octyl-\(\beta\)-glucopyranoside (Boehringer Mannheim, Indianapolis, IN), 50 mM Tris-HCl, pH 7.4, and 1 mM MnSO\(_4\). Protease inhibitors (1 mM phenylmethylsulfonyl fluoride, 2 \(\mu\)g/ml aprotinin, and 10 mM N-ethylmaleimide) (Sigma) were added during solubilization and throughout the subsequent procedures. The extract was then centrifuged for 10 minutes at 2000 \(g\) followed by 15 minutes at 15 000 \(g\). The supernatant of the solubilized whole cell extract was used for immunoprecipitation or affinity chromatography.

**Affinity Chromatography**

Affinity columns were prepared by coupling the ligand (BSA, type I collagen, type IV collagen, laminin) to CNBr-activated Sepharose (Pharmacia, Pleasant Hill, CA). The fibronectin affinity column was made from the 120 kD fragment of fibronectin.\(^{39}\) The solubilized whole cell extract from six confluent 10-cm plates of RASM cells was applied to a BSA-Sepharose precolumn (1 cm x 1 cm) previously equilibrated with 50 mM octylglucoside, 50 mM Tris-HCl, pH 7.4, 1 mM MnSO\(_4\), 1 \(\mu\)g/ml BSA, and 0.005% Na\(_2\)EDTA (Wash Buffer A). The BSA-Sepharose precolumn was eluted with four column volumes of Wash Buffer A. The eluate from the BSA-Sepharose precolumn was passed repeatedly through a substrate-Sepharose column (1 cm x 2 cm) over a 1.5-hour period. The substrate-Sepharose column was then washed with five column volumes of Wash Buffer A. Bound receptors were eluted first with eight column volumes of 0.2 M NaCl in Wash Buffer A; second, with five column volumes of 10 mM EDTA in Wash Buffer A without divalent cations; and finally, with six column volumes of 1 M NaCl in Wash Buffer A. The substrate-Sepharose columns (fibronectin, laminin, type I, and type IV collagen) were reused up to five times. Twenty-two microliters of 1 M MgCl\(_2\) was added immediately to each 1 ml fraction of the EDTA eluate.

**Immunoprecipitation**

Whole cell extracts in solubilization buffer and column eluates were first pre-cleared by incubating 1 ml of the whole cell extract or column eluate with 50 \(\mu\)l of either packed protein A-Sepharose beads (for anti-hamster \(\beta\)s, serum or anti-\(\alpha\)s serum) (Sigma) or goat-antimouse IgG\(_2\)a-Sepharose (for 3A3) for 1 hour at 4°C, then centrifuging the mixture. Next, either 10 \(\mu\)l of anti-hamster \(\beta\)s serum or anti-\(\alpha\)s serum, or 3.5 \(\mu\)g of 3A3 MAb was added to the 1 ml supernatants and incubated for 2 hours at 4°C. Immune complexes were recovered by incubating the supernatants for 2 hours with 50 \(\mu\)l of either packed protein A-Sepharose or goat-antimouse IgG\(_2\)a-Sepharose. The beads with bound immune complexes were washed as described.\(^{36}\) Control immunoprecipitation performed with pre-immune normal goat serum, normal rabbit serum, or irrelevant mouse MAb produced negligible radioactivity.

**Electrophoresis**

Eluates from the affinity columns and samples from the immunoprecipitation experiments were analyzed by SDS-PAGE according to the method of Laemmli.\(^{40}\) Samples were solubilized in sample buffer, reduced with 5% 2-mercaptoethanol, and heated at 100°C for 4 minutes. Nonreduced samples were treated as above except that 10 mM N-ethylmaleimide was substituted for 2-mercaptoethanol. The samples were separated on 6% polyacrylamide gels and detected by autoradiography. Prestained protein standards (Sigma) were used to calculate the apparent molecular mass and consisted of \(\alpha\)lactalbumin (180 kD), \(\beta\)-galactosidase (116 kD), fructose-6-phosphate kinase (84 kD), pyruvate kinase (58 kD), fumarase (48.5 kD), lactate dehydrogenase (36.5 kD), and triosephosphate isomerase (26.6 kD).

**Results**

**Cell Adhesion Studies**

RASM cells adhered to wells coated with the ECM substrates (laminin, fibronectin, collagen types I and IV) as well as the non-ECM substrates (poly-L-lysine and wheat germ agglutinin). In contrast, the cells failed to attach to wells coated with BSA (Figure 1).

We had previously found that anti-hamster \(\beta\)s serum inhibits RASM cell adhesion to ECM-derived substrates in a concentration-dependent manner (R.I. Clyman et al., unpublished observations). In the current experiment, anti-hamster \(\beta\)s serum at a concentration of 1% inhibited cell adhesion to fibronectin and to collagen types I and IV by greater than 90% and inhibited adhesion to laminin by 55% (Figure 1). The inhibition produced by anti-hamster \(\beta\)s serum was specific for ECM-derived substrates; attachment to poly-L-lysine was not affected by the anti-serum. A 1% concentration of anti-hamster \(\beta\)s serum did inhibit attachment of RASM cells to wheat germ agglutinin; however, RASM cell attachment to wheat germ agglutinin was also inhibited by a 1% concentration of pre-immune goat serum, suggesting that this inhibition was due to competition by the sialoglycoproteins (data not shown).

The MAb 3A3 inhibited initial attachment of RASM cells to several of the immobilized substrates (Figure 1). Concentrations of 3A3 as low as 5 \(\mu\)g/ml inhibited cell attachment to collagen type IV to the same degree as the anti-hamster \(\beta\)s serum. 3A3 also inhibited RASM cell attachment to collagen type I and laminin but was not as effective in its inhibition as the anti-hamster \(\beta\)s serum. In contrast to its effects on laminin and collagen types I and IV, 3A3 had no inhibitory effect on the cell adhesion to...
Figure 1. Effect of anti-hamster β1 serum and MAb 3A3 on rat aortic smooth muscle cell attachment to extracellular matrix proteins. Cells were labeled with 125I-UdR and were plated into wells precoated with bovine serum albumin (BSA) (1 mg/ml), fibronectin (FN) (8.75 μg/ml), laminin (LN) (20 μg/ml), poly-L-lysine (PLL) (10 μg/ml), or wheat germ agglutinin (WGA) (10 μg/ml). The assay was performed in the presence of control medium, anti-hamster β1 serum (diluted 1:100), and 3A3. The cells were allowed to attach to the wells for 15 minutes at 37°C. The percentage of cells adhering to BSA-coated wells was 0±0%. Values represent the mean percentages (±SD) of the radioactivity that adhered to the well in triplicate wells. This experiment was repeated twice with similar trends.

Identification of 3A3 Antigen in RASM Cells

Numerous radiolabeled proteins were identified when whole cell detergent extracts were analyzed by SDS-PAGE (Figure 2). When the extracts were immunoprecipitated with anti-hamster β1 serum, a limited series of major, closely migrating proteins with apparent molecular masses centered at 120, 130 to 150, 165, and 185 kD (nonreduced) were observed (Figure 2). We have previously shown that the anti-hamster β1 serum specifically recognizes the 120 kD protein; therefore, the other bands probably represent different α subunits that have been co-precipitated with the β1 integrin protein (R.I. Clyman et al., unpublished observations).

When the detergent extracts were immunoprecipitated with MAb 3A3, only two protein bands were observed; these were centered at 120 and 185 kD (Figure 2). When the extracts that were precipitated with MAb 3A3 were examined under reducing conditions, the 120 kD β1 subunit exhibited decreased mobility; this is typical for the β subunit of the integrin class of cell surface receptors and suggests the presence of multiple intramolecular disulfide-rich domains in this protein band. Under reducing conditions, there was also decreased mobility of the protein band at 185 kD (to 190 kD).

3A3 Antigen Binds to Collagen Type IV

125I-labeled proteins eluted from a collagen type IV-Sepharose column were identified by SDS-PAGE and autoradiography (Figure 3A). When the collagen type IV-Sepharose column was eluted with EDTA, two polypeptides were recovered with apparent molecular mass (nonreduced) of 120 and 185 kD. This set of proteins was recognized by the anti-hamster β1 serum (unpublished data) and appeared to correspond to the 120 kD and 185 kD bands seen on the immunoprecipitation of the whole cell extract (Figure 2). Most importantly, this heterodimer protein complex was specifically recognized by MAb 3A3 (Figure 3A).
3A3 Antigen Binds to Collagen Type I

When $^{125}$I-labeled cell extracts were loaded onto a type I collagen-Sepharose affinity column, a different elution pattern was obtained. Anti-hamster $\beta_1$ serum recognized four bands that were eluted from the type I collagen-Sepharose column with EDTA: two major bands at 185 and 120 kD and two minor bands at 167 and 150 kD (nonreduced) (Figure 3B). In contrast to the minor band at 150 kD, which was consistently immunoprecipitated from the EDTA eluate by anti-hamster $\beta_1$ serum, the 167 kD band was observed only infrequently. Upon reduction, the 185 and 120 kD bands shifted to 190 and 140 kD, respectively. In addition, the band at 150 kD shifted to 160 kD, and the band at 167 kD moved up to 175 kD (Figure 3B). The MAb 3A3 precipitated only two of the four proteins immunoprecipitated by the anti-hamster $\beta_1$ serum: the 185 and 120 kD (nonreduced) bands.

3A3 Antigen Binds to Laminin

When the laminin-Sepharose column was eluted with EDTA, numerous polypeptide bands were observed (Figure 4A). However, only four bands were recognized by MAb 3A3 (Figure 4B). These bands were not recognized by MAb 3A3 (Figure 4B).

Discussion

The data presented in this paper provide strong evidence for the existence of an $\alpha_\gamma/\beta_1$-like integrin cell surface receptor that mediates RASM cell attachment to laminin and to collagen types I and IV. We have previously identified a series of $\beta_1$-associated $\alpha$ subunits on RASM cells that appear to control cell adhesion to fibronectin, laminin, and collagen types I and IV (R.I. Clyman et al., unpublished observations). In the current series of experiments, we have used a MAb, 3A3, that inhibits RASM cell adhesion to laminin and collagen types I and IV to identify the proposed laminin-collagen receptor. 3A3 immunoprecipitated two protein bands from detergent extracts of RASM cells. These two proteins were also recognized by anti-hamster $\beta_1$ serum, suggesting that they constitute a heterodimeric receptor of the integrin family. In addition, the two polypeptides recognized by MAb 3A3 selectively bound to laminin- and collagen-types I and IV affinity columns (with dependence on divalent cations). The heterodimer complex (185/120 kD), recognized by both anti-hamster $\beta_1$ serum and 3A3, was the only $\beta_1$ integrin eluted from the collagen type IV-Sepharose column (Figure 3A). This $\beta_1$ receptor complex appeared to play a major role in mediating RASM cell attachment to type IV collagen because anti-hamster $\beta_1$ serum completely blocked adhesion to collagen type IV (Figure 1). Similarly, 3A3, which appears to react with an epitope either on the high molecular weight $\alpha_\gamma$ subunit$^{22}$ or on the $\alpha_\gamma/\beta_1$ complex, also eliminated the initial adhesion of RASM cells to collagen type IV. It is unlikely that antibody-induced cytotoxicity was involved because, in the presence of either 3A3 or anti-hamster $\beta_1$ serum, the RASM...
Figure 3. Affinity chromatography of detergent-solubilized rat aortic smooth muscle cells on collagen type IV-(A) and type I-(B) Sepharose columns and SDS-PAGE (6%) analysis of column eluates. A. Proteins eluted from the type IV collagen-Sepharose column with 10 mM EDTA were immunoprecipitated with 3A3. Both the original sample (Lanes 1 and 2) and the immune complex (Lane 3) were examined under nonreducing (Lanes 1 and 3) and reducing (Lane 2) conditions. B. Proteins eluted from the type I collagen-Sepharose column with 10 mM EDTA were immunoprecipitated with 3A3 and anti-hamster β1 serum. Both the original sample (Lanes 4 and 7) and the 3A3 (Lanes 5 and 8) and anti-hamster β1 serum (Lanes 6 and 9) immune complexes were examined under nonreducing (Lanes 4 to 6) and reducing (Lanes 7 to 9) conditions. Molecular mass markers (in kilodaltons) are shown on the left.

Figure 4. Affinity chromatography of detergent-solubilized rat aortic smooth muscle cells on laminin-(A) and fibronectin-(B) Sepharose columns and SDS-PAGE (6%) analysis of column eluates. A. Proteins eluted from the laminin-Sepharose column with 10 mM EDTA were immunoprecipitated with 3A3 and anti-hamster β1 serum. Both the original sample (Lanes 1 and 4) and the 3A3 (Lanes 2 and 5) and anti-hamster β1 serum (Lanes 3 and 6) immune complexes were examined under nonreducing (Lanes 1 to 3) and reducing (Lanes 4 to 6) conditions. B. Proteins eluted from the fibronectin-Sepharose column with 10 mM EDTA were immunoprecipitated with 3A3 and a rabbit antiserum to the cytoplasmic domain of the αv integrin subunit. Both the original sample (Lanes 1 and 4) and the 3A3 (Lanes 2 and 5) and anti αv serum (Lanes 3 and 6) immune complexes were examined under nonreducing (Lanes 1 to 3) and reducing (Lanes 4 to 6) conditions. Molecular mass markers (in kilodaltons) are shown on the left.
cells were able to attach to the non-ECM substrate poly-L-lysine.

The 185 kD α subunit has approximately the same SDS-PAGE mobilities in both reducing and nonreducing conditions as the α subunit of the very-late-activation antigen (VLA)-1 (αβ1) heterodimer that has been characterized in human cell lines. In addition, partial sequencing of the high molecular weight polypeptide recognized by 3A3 in rat PC12 cells has identified this α subunit as the rat homolog of the human VLA-1.41 Recently the VLA-1 integrin dimer from human vascular smooth muscle cells has been found to bind both collagen type I and type IV as well as laminin (R.I. Clyman et al., unpublished observations).

In addition to the 185/120 kD heterodimer complex recognized by 3A3, at least one other α subunit (150 kD, nonreduced) was eluted from the collagen type I-Sepharose column and was precipitated by the anti-hamster β1 serum (Figure 3B). The RASM cell 150 kD protein has approximately the same SDS-PAGE mobility pattern under both reducing and nonreducing conditions as the α subunit of the αβ1 heterodimer that has been characterized in human cell lines.22 In the past, the αβ1 receptor has been found to bind to both collagen type I and type IV.α,β.Note that the presence of other αβ integrin receptors for collagen type I enabled the RASM cells to adhere to collagen type I even though the site on the 185/120 kD receptor that is recognized by 3A3 had been blocked.

The anti-hamster β1 serum immunoprecipitated four polypeptides from the eluates of the laminin-Sepharose columns. In addition to the 185/120 kD receptor complex recognized by 3A3, there were additional polypeptides with mobilities of 100 KD (reduced) and 60 KD (reduced). While the 100 kD (reduced) band appeared to be similar to the αβ1 subunit seen in human melanoma cells,7 (R.I. Clyman et al., unpublished observations), additional studies will be needed to characterize this band and the 60 kD (reduced) band.

The anti-hamster β1 serum inhibited 55% of the RASM cell binding to laminin, which suggests that β1 integrins are important (if not essential) in mediating cell adhesion to laminin. In contrast, 3A3 was able to block initial adhesion to laminin by only 16%. It would appear that having other β1 integrin receptors for collagen type I enabled the RASM cells to adhere to collagen type I even though the site on the 185/120 kD receptor that is recognized by 3A3 had been blocked.

The anti-hamster β1 serum inhibited 55% of the RASM cell binding to laminin, which suggests that β1 integrins are important (if not essential) in mediating cell adhesion to laminin. In contrast, 3A3 was able to block initial adhesion to laminin by only 16%. Therefore, just as we saw when RASM cells adhered to collagen type I, the presence of other β1 integrin receptors for laminin enables the RASM cells to adhere to laminin despite blockade of the site on the 185/120 kD receptor that is recognized by 3A3. These findings in RASM cells are in sharp contrast to those observed in PC12 cells, a rat neuronal cell line.38 3A3 was able to inhibit 90% of the adherence of PC12 cells to laminin.29 It would appear that PC12 cells may be similar to another rat neuronal cell line, B50, which possesses only one β1 integrin laminin receptor with an α subunit that behaves like α5.32

In contrast to the above studies using laminin- and collagen-affinity columns, the 185/120 kD complex recognized by 3A3 failed to bind to fibronectin-Sepharose columns. Instead, the classical fibronectin receptor, was the only β1 integrin recovered from the fibronectin-affinity column. As one would anticipate from the affinity chromatography results, anti-hamster β1 serum completely blocked RASM cell adhesion to fibronectin, while 3A3 had no effect.

ECM receptors on smooth muscle cells provide a means for regulating the smooth muscle cell migration that occurs after injury to the arterial wall. Members of the β1 family of integrin receptors appear to mediate RASM cell attachment to ECM components. We have identified an αβ1-like receptor that mediates adhesion to several structurally diverse, ECM molecules like laminin and collagen types I and IV. This receptor appears to be the only β1 integrin receptor mediating RASM cell adhesion to type IV collagen. On the other hand, RASM cells have other β1 integrin receptors, in addition to the αβ1-like receptor, that can be used to attach to laminin and collagen type I. As a result, inhibition of the αβ1-like receptor has only a small effect on RASM cell adhesion to these ECM substrates. Further studies will reveal what role these other β1 integrin receptor complexes have in the adhesion process.

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