Regulated adherence of polymorphonuclear leukocytes (PMNs) to endothelium and subendothelial matrix is a critical event for PMN localization at and migration into inflammatory sites. We previously reported that human PMNs stimulated in vitro adhere to laminin, the major glycoprotein of mammalian basement membrane, by both CD11/CD18 (β2 integrin)-dependent and CD11/CD18-independent mechanisms. This CD11/CD18-independent adherence is inhibited by monoclonal antibodies (MoAbs) directed against the β subunit of integrins (very late antigens [VLA]). The specific PMN VLA receptor responsible for stimulated CD11/CD18-independent PMN adherence to laminin was not elucidated. We show here that this CD11/CD18-independent adherence is mediated by a member of the β integrins, VLA-6. MoAbs against the α, subunit of integrins (CD11c) and a common β chain (CD18). Less is known about the molecular mechanisms involved in PMN adhesion to connective tissue proteins in the subendothelial basement membrane.

PMN surface adhesion molecules are rapidly altered in response to specific stimuli to mediate adherence to a variety of substrates. The best characterized membrane adhesion molecules on PMNs are the CD11/CD18. The CD11/CD18 complex consists of three heterodimeric receptors, also known as the LFA-1, CR3, and p150,95, each with a separate α chain (CD11α) and a common β chain (CD18). The β chain is one of five or more β chains (βi) identified in a larger family of related cell surface heterodimers, called the integrins, that are involved in cell-cell and cell-protein interactions. A considerable body of experimental and clinical evidence suggests that the CD11/CD18 glycoprotein complex plays a critical role in stimulated PMN adherence because monoclonal antibodies (MoAbs) directed against CD11/CD18 inhibit stimulated PMN adhesion in vitro to endothelial cells and to a variety of protein surfaces, and because PMNs from patients whose leukocytes congenitally lack CD11/CD18 integrins (leukocyte adhesion deficiency) exhibit poor or absent adherence in vitro and poor or absent accumulation of PMNs at inflammatory sites in vivo.

We have recently investigated PMN adherence in vitro to laminin, the major glycoprotein of mammalian basement membrane. We found that while unstimulated human PMNs exhibited low basal adherence to laminin-coated plastic, PMNs can be stimulated to adhere to laminin by a variety of agonists. After stimulation with phorbol myristate acetate (PMA), PMN adherence to laminin and laminin-containing subendothelial matrices was partially inhibited by MoAb directed against the β subunit of the CD11/CD18. Our studies also showed, however, that stimulated PMNs adhere to laminin through a non-CD11/CD18 receptor or receptors, because anti-CD18 MoAb does not completely inhibit stimulated adherence to laminin and because stimulated PMNs from a patient with CD11/CD18 deficiency exhibit significant, although reduced, adherence to laminin. Taken together, these data suggested that laminin is a ligand for CD11/CD18, but also that a separate, CD11/CD18-independent PMN adherence receptor for laminin is functionally expressed after PMN activation. The CD11/CD18-independent PMN adherence to laminin was shown to be mediated by a member of the β, (very late antigens [VLA]) integrins because anti-β MoAbs inhibited CD11/CD18-independent PMN adherence to laminin. These data showed that PMNs possess two classes of adherence receptors whose functional activity is upregulated after PMN stimulation: the well-characterized CD11/CD18 receptors, and members of the β class of integrin receptors whose presence and function on PMNs has been largely undefined.

VLA-6 (α5β1), one of six VLA integrins, is present on a variety of cells. VLA-6 mediates platelet adhesion to laminin in the absence of platelet activation, while activation of macrophages with phorbol esters is required for macrophage VLA-6 to mediate adherence to laminin. Laminin and the bacterial protein invasin are the only ligands thus far identified for VLA-6, and VLA-6 has not been previously described to be present on PMNs.
this study, we show that the PMN \( \beta_1 \) receptor for laminin is VLA-6.

**MATERIALS AND METHODS**

**Buffers and reagents.** Human serum albumin (HSA) for infusion (Cutter Biologicals, Berkeley, CA), PMA (Sigma Chemical Co, St Louis, MO), and gelatin (Type II from swine skin; Fisher Scientific, Pittsburgh, PA) were purchased. Murine laminin purified from the EHS sarcoma was a gift from Dr Hynda Kleinman (National Institute of Dental Research, Bethesda, MD). Hank’s Buffered Salt Solution containing 1.2 mmol/L Ca\(^{2+} \) and 0.8 mmol/L Mg\(^{2+} \) (HBSS) was purchased from M.A. Bioproducts (Walkersville, MD).

**Antibodies.** Murine MoAbs IB4 (IgG2a),\(^{20} \) 60.1 (IgG2a),\(^{20} \) W6/32 (IgG2a),\(^{20} \) 450-30 (IgG1),\(^{20} \) 3D9 (IgG1),\(^{20} \) and S1 (IgG1)\(^{20} \) bind to the \( \beta \) chain of CD11/CD18 (CR3), a common determinant of HLA class I, \( \alpha \) and \( \beta \) subunits of the VLA-6, the complement receptor for C3b (CR1), and the \( \alpha \) and \( \beta \) subunits of glycophorin IIb/IIa, respectively. GoH3,\(^{20} \) MoAb 13, and MoAb 16 are rat MoAbs (IgG2a) that bind to the \( \alpha \) and \( \beta \) subunits of the VLA integrins, respectively. BIVF2 and ES46.8 are rat isotype-matched control MoAbs (IgG2a). The MoAbs used in this report are summarized in Table 1.

**PMN adherence assay.** The method for determining PMN adherence to protein-coated plastic wells and to endothelial cell monolayers has been previously described in detail.\(^{4,5,37} \) PMNs were obtained from healthy adult donors, or from a patient with severe leukocyte adhesion deficiency (CD11/CD18 deficiency). PMNs from this patient completely lack detectable CD11/CD18 (severe phenotype) as determined using flow cytometry or by immunoprecipitation of surface-labeled proteins with MoAb IB4 to detect the \( \beta \) chain of the CD11/CD18 complex. PMNs were isolated from heparinized blood by dextran sedimentation, hypotonic lysis, and Ficoll-Hypaque density gradient centrifugation, as previously described.\(^{34,37} \) PMNs were then aspirated and washed once with HBSS just before the addition of protein-coated wells. PMNs were then incubated with MoAb for 10 minutes at room temperature before addition to the wells. MoAbs were present throughout the course of the incubation.\(^{114} \) PMNs (225 \( \mu \))L were added to the wells followed by the addition of 25 \( \mu \)L of the different agonists. The PMNs were then allowed to adhere for 30 minutes at 37\(^{\circ} \)C, and nonadherent cells were then removed by gentle aspiration and one wash with 0.5 mL HBSS. Nonadherent cells were saved and radioactivity was quantitated. Counts associated with adherent cells were recovered by two cycles of lysis with 1 mol/L N\(_2\)H\(_4\),OH and vigorous scraping with a cotton tip applicator. The percentage of adherent cells was calculated as a percentage of the total number of counts added to each well.

**Platelet preparation.** Blood was drawn from normal adult volunteers directly into 0.01 mol/L EDTA and centrifuged at 400g for 15 minutes to remove red and white blood cells. The platelet-rich plasma was then washed three times in PBS containing 0.001 mol/L EDTA and counted in an electronic counter (Coulter Electronics, Hialeah, FL).

**Flow cytometry.** Purified PMNs or platelets were incubated with MoAbs for 30 minutes on ice, washed twice, and then incubated with fluorescein-labeled goat antirabbit or goat antimouse antibody for an additional 30 minutes on ice. The cells were then washed, fixed with phosphate-buffered saline (PBS) containing 2% paraformaldehyde, and analyzed on an Ortho Cytofluorograph II (Ortho Diagnostics, Inc, Westwood, MA). Immunoprecipitation of \( ^{125} \)I-surface-labeled PMNs and platelets. Purified human PMNs or platelets were suspended in PBS and surface labeled using Na\(^{22} \)I and chloroglycouril\(^{22} \) (Sigma). After labeling, cells were washed four times with PBS containing 2 mmol/L KI, and solubilized in 0.01 mol/L Tris, 0.145 mol/L NaCl, pH 7.4, containing 0.5 mmol/L EDTA, 25 \( \mu \)mol/L para-nitrophenyl-para-guanidinobenzoate, 1 mmol/L di-isopropyl-fluorophosphate, 1 mmol/L phenylmethylsulfonylfluoride, 2 \( \mu \)g/mL aprotinin, and 2 \( \mu \)g/mL leupeptin (lysis buffer) for 30 minutes at 37\(^{\circ} \)C. After the solubilization, the lysates were centrifuged for 10 minutes at 12,000g to remove insoluble material, and precleared successively with Sepharose 4BCL and Protein A-Sepharose. Aliquots of precleared cell lysates were mixed with GoH3 (3 \( \mu \))g for 1 hour at 4\(^{\circ} \)C. Immune complexes were precipitated with 25 \( \mu \)g of rabbit antirabbit IgG (Sigma) bound to 25 \( \mu \)L of Protein A-Sepharose. After mixing for 2 hours at 4\(^{\circ} \)C, the precipitates were extensively washed with lysis buffer, and the pellets were boiled in sample buffer for preparation for sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). SDS-PAGE was performed according to the method of Laemmli et al\(^{39} \) using a 7% resolving gel and 4% stacking gel. Reduced samples were treated with 2% 2-mercaptoethanol.

Immunoprecipitation of platelet VLA-6 was also performed in the presence of lysed PMNs. In these experiments, \( ^{125} \)I-surface-labeled platelets were lysed in the presence of 5 \( \times 10^7 \) unlabeled PMNs. Preabsorption and immunoprecipitation of the VLA-6 with GoH3 was then performed as described above.

**Two-dimensional electrophoresis of immunoprecipitated proteins.** Immunoprecipitates were analyzed by two-dimensional gel electrophoresis using the method of O’Farrell.\(^{40} \) First dimensional isoelectric focusing was performed in 5% acrylamide tube gels using a mixture of pH 3-10 and pH 5-7 Ampholines (LKB, Bromma, Sweden) in a ratio of 2:3. The second dimension was performed on 7% SDS-PAGE. Replicate tube gels were cut into 1-cm slices and placed in 2 mL of distilled water to determine the pH gradient in the isoelectric focusing.

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**Table 1. MoAbs Used in These Studies**

<table>
<thead>
<tr>
<th>MoAb</th>
<th>Species</th>
<th>Subclass</th>
<th>Antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td>IB4</td>
<td>Mouse</td>
<td>IgG2a</td>
<td>CD18</td>
</tr>
<tr>
<td>60.1</td>
<td>Mouse</td>
<td>IgG2a</td>
<td>CD11b</td>
</tr>
<tr>
<td>W6/32</td>
<td>Mouse</td>
<td>IgG2a</td>
<td>HLA Class I</td>
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<tr>
<td>450-30</td>
<td>Mouse</td>
<td>IgG1</td>
<td>( \alpha_4 )</td>
</tr>
<tr>
<td>3D9</td>
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<td>IgG1</td>
<td>CR1</td>
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<tr>
<td>GoH3</td>
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<td>( \alpha_4 )</td>
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<td>IgG2a</td>
<td>( \beta_1 )</td>
</tr>
<tr>
<td>MoAb 16</td>
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<td>IgG2a</td>
<td>( \alpha_4 )</td>
</tr>
<tr>
<td>ES46.8</td>
<td>Rat</td>
<td>IgG2a</td>
<td>( \beta_1 ) cytoplasmic</td>
</tr>
<tr>
<td>BIVF2</td>
<td>Rat</td>
<td>IgG2a</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

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Table 2. Anti-VLA-6 MoAbs Inhibit CD11/CD18-independent PMN adherence to laminin

<table>
<thead>
<tr>
<th>Agonist</th>
<th>MoAb†</th>
<th>% Adherence§</th>
<th>Significance$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buffer</td>
<td></td>
<td>10.2 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>PMA</td>
<td>IB4</td>
<td>67 ± 5</td>
<td></td>
</tr>
<tr>
<td>PMA</td>
<td>60.1</td>
<td>60.9 ± 6</td>
<td></td>
</tr>
<tr>
<td>PMA</td>
<td>IB4 + 60.1</td>
<td>31.0 ± 8</td>
<td></td>
</tr>
<tr>
<td>PMA</td>
<td>IB4 + 60.1 + GoH3</td>
<td>10.0 ± 8</td>
<td>P &lt; .01</td>
</tr>
<tr>
<td>PMA</td>
<td>IB4 + 60.1 + 450-30</td>
<td>12.3 ± 7</td>
<td>P &lt; .01</td>
</tr>
<tr>
<td>PMA</td>
<td>IB4 + 60.1 + MoAb 13</td>
<td>7.9 ± 7</td>
<td>P &lt; .01</td>
</tr>
<tr>
<td>PMA</td>
<td>IB4 + 60.1 + ES46.8</td>
<td>25.9 ± 4</td>
<td>NS</td>
</tr>
<tr>
<td>PMA</td>
<td>IB4 + 60.1 + BIVF2</td>
<td>35.6 ± 7</td>
<td>NS</td>
</tr>
<tr>
<td>PMA</td>
<td>IB4 + 60.1 + MoAb 16</td>
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<td>NS</td>
</tr>
<tr>
<td>PMA</td>
<td>IB4 + 60.1 + 3D9</td>
<td>29.2 ± 6</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviation: NS, not significant.
*PMA was present at a final concentration of 10 ng/mL.
†All MoAb concentrations were at 10 μg/mL except GoH3 and BIVF2, which were present at 3 μg/mL.
‡Percent adherence of PMNs to laminin after 30 minutes of incubation determined as described in Materials and Methods, and expressed as mean ± SD.
§Significance compared with PMA + IB4 + 60.1 as determined by Student’s t-test.

RESULTS

Anti-VLA-6 MoAbs inhibit CD11/CD18-independent PMN adherence to laminin. As we previously reported,14 unstimulated human PMNs exhibit low, basal adherence to plastic wells coated with a laminin (Table 2). Addition of PMA at 10 ng/mL to the adherence assay markedly stimulates PMN adherence to the laminin-coated surface, and this stimulated adhesion is only partially inhibited by the anti-β1 MoAb IB4 or by the anti-CD11b MoAb 60.1 (Table 2). Together, MoAbs IB4 and 60.1 blocked CD11/CD18-dependent adherence better than either alone (Table 2), and reduced stimulated PMN adherence to laminin to a level (31% ± 7%) approximately equal to that of PMNs from CD11/CD18-deficient patient (27% ± 6%, see Fig 2). Addition of the anti-αv MoAbs GoH3 or 450-30, or the anti-β1 MoAb 13, completely inhibited stimulated CD11/CD18-dependent adherence to laminin when IB4 and 60.1 were used to block CD11/CD18-dependent adherence. A variety of control MoAbs did not inhibit CD11/CD18-independent PMN adherence to laminin (Table 2).

Significant inhibition of CD11/CD18-independent adhesion was detectable when 450-30 was present at concentrations as low as 3 μg/mL, with complete inhibition of CD11/CD18-independent adhesion occurring at concentrations of 10 μg/mL or greater (Fig 1). No inhibition of PMA-stimulated adherence occurred when adherence was performed in the presence of 450-30 alone at concentrations as high as 30 μg/mL (Fig 1). This result is similar to our previous finding that anti-β1 MoAbs do not affect PMA-stimulated adherence to laminin unless CD11/CD18-dependent adhesion is inhibited or absent.14

We previously showed that PMA-stimulated PMNs from a patient with CD11/CD18 deficiency adhere to laminin,14 an observation that confirms that PMNs can adhere to laminin by CD11/CD18-independent mechanisms. Therefore, we tested the ability of GoH3 to inhibit stimulated adherence of CD11/CD18-deficient PMNs to laminin. PMA stimulated approximately a fourfold increase in the adhesion of CD11/CD18-deficient PMNs to laminin, confirming the presence of a CD11/CD18-independent mechanism for PMN adhesion to laminin. This stimulated adherence to laminin is completely inhibited by GoH3 (Fig 2). In contrast, control MoAbs BIVF2, ES46.8, and MoAb 16 did not inhibit adherence of CD11/CD18-deficient PMNs to laminin (Fig 2). Thus, VLA-6 mediates CD11/CD18-independent PMN adherence to laminin.

Analysis of PMN VLA-6 by flow cytometry. The VLA-6 receptor has not previously been described on human PMNs. Analysis by flow cytometry, however, shows that anti-VLA-6 MoAbs GoH3 and 450-30 both bind to human PMNs (Fig 3). The density of the αv subunit of the VLA integrins on PMNs is lower than that of β2 subunit of the CD11/CD18, as determined by staining with the anti-β2 MoAb IB4 (Fig 3).

It seemed unlikely that the VLA-6 detected on PMNs was due to platelet contamination, because visible platelet contamination is not found in our preparations of PMNs when examined by light microscopy. Furthermore, the platelet glycoprotein IIb/IIIa was not detected on PMNs by MoAb S1, which specifically binds the IIb subunit of the major platelet glycoprotein IIb/IIIa (Fig 3). This finding indicates that VLA-6 is a PMN integral protein, and that its detection is not due to contamination with platelets or platelet fragments.
Immunoprecipitation of PMN VLA-6. Purified platelets and PMNs were surface-labeled with 125I, solubilized, and immunoprecipitated with GoH3. Analysis by SDS-PAGE under nonreducing conditions showed the two-chain structure of the platelet VLA-6, with the α, chain migrating on SDS-PAGE with an apparent molecular weight (Mr) of 150 Kd, and the β, chain migrating with an Mr of 120 Kd. Upon reduction, the platelet α, chain reduces in size and comigrates with the β, chain with an Mr of 130 Kd (Fig 4). In contrast, GoH3 immunoprecipitates from PMNs migrate as a broad band with Mr 120 to 150 Kd under both reduced and nonreduced conditions. A more discrete band is identified within this broad band that is the same size as the platelet α, subunit is not immunoprecipitated by MoAb directed against the β, subunit while both the α, and the β, subunits are immunoprecipitated by MoAb directed against α, (Fig 5). The band seen in the anti-β, immunoprecipitates from platelets at Mr 150 Kd and pl 5.2 is the α, subunit of platelet VLA-2, as previously documented by Hemler et al.
The band seen in the anti+ immunoprecipitates from platelets at Mr 150 Kd and pl 5.2 is the α, subunit of platelet VLA-2, as previously documented by Hemler et al.

VLA-6 immunoprecipitated from surface-labeled platelet lysates that had been incubated with unlabeled PMN lysates were identical to platelet VLA-6 that had not been exposed to PMN lysates (Fig 4, lanes 1 and 2). Therefore, the distinct appearance of the PMN VLA-6 is not due to degradation of the VLA-6 by PMN proteases, or to other artificial alterations in the apparent Mr, eg, from contamination with PMN nuclear material. Taken together, these data show that the PMN β, exhibits heterogeneity in molecular mass and accounts for the broadly migrating band seen in the VLA-6 immunoprecipitates.

**DISCUSSION**

PMNs are circulating leukocytes that participate in inflammation in the extravascular compartment. For PMNs to enter the extravascular compartment, PMNs must adhere to and crawl over and through various substrates,
including endothelium, subendothelial basement membrane, and extracellular matrix molecules of the extravascular space. It is therefore likely that PMNs possess specific receptors for extracellular matrix macromolecules. We recently reported that activated PMNs possess at least two different mechanisms for adherence to laminin, the major glycoprotein of subendothelial basement membrane, and that one of these mechanisms involves the β1 integrins. Originally thought to be absent from PMNs, β1 integrins have more recently been reported to be expressed on PMNs, although the α chains associated with PMN β1 integrins and the functions of these integrins on PMNs have not been well-defined. In the studies reported here, we show that the α6 subunit of VLA-6 is detectable on PMNs by flow cytometry and by immunoprecipitation of surface-labeled PMNs. This finding suggested that VLA-6 (α6β1) is present on human PMNs because we have previously shown β1 on PMNs. This was confirmed by one- and two-dimensional analysis of PMN and platelet immunoprecipitates that showed α6β1 in anti-α6 immunoprecipitates from PMNs. PMN α6 was found to be identical to the platelet α6 chain on the basis of Mr and pI, while the PMN β1 differs somewhat from the platelet β1 in Mr. We previously showed that anti-β1 MoAbs immunoprecipitate a single broad band from PMNs with an Mr of approximately 135 Kd. The appearance of this band immunoprecipitated from PMNs is distinctly different from the anti-β1 immunoprecipitated from platelets, which appears as a discrete band with Mr of 120 Kd. The two-dimensional gel analysis of the anti-β1 and anti-α6 immunoprecipitates from PMNs shown in this report shows that the PMN β1 is slightly larger and has a greater heterogeneity in mass than the platelet β1 chain.

These data not only establish the presence of VLA-6 on PMNs, but also show that the PMN VLA-6 can function in vitro as an adherence receptor for laminin. Our previous studies showed that stimulated PMNs adhere to laminin by mechanisms that are both CD11/CD18-dependent and VLA-dependent. We show here that the VLA integrin responsible for this CD11/CD18-independent adherence is VLA-6 because the anti- VLA-6 MoAbs GoH3 and 450-30 completely inhibit stimulated PMN adherence when anti-CD11/CD18 MoAbs are used to block CD11/CD18-dependent adherence, or when CD11/CD18 is congenitally absent from the PMN. Neither anti-β1 nor anti-α6 MoAbs detectably inhibit PMA-stimulated PMN adherence to laminin when used alone because demonstration of VLA-dependent adherence requires that the CD11/CD18 be at least partially inhibited under the conditions used in this assay. The most plausible explanation for these results is that the contribution of the VLA-6 to PMN adherence to laminin when used alone because demonstration of VLA-dependent adherence requires that the CD11/CD18 be at least partially inhibited under the conditions used in this assay. The most plausible explanation for these results is that the contribution of the VLA-6 to PMN adherence to laminin when used alone because demonstration of VLA-dependent adherence requires that the CD11/CD18 be at least partially inhibited under the conditions used in this assay. The most plausible explanation for these results is that the contribution of the VLA-6 to PMN adherence to laminin when used alone because demonstration of VLA-dependent adherence requires that the CD11/CD18 be at least partially inhibited under the conditions used in this assay. The most plausible explanation for these results is that the contribution of the VLA-6 to PMN adherence to laminin when used alone because demonstration of VLA-dependent adherence requires that the CD11/CD18 be at least partially inhibited under the conditions used in this assay. The most plausible explanation for these results is that the contribution of the VLA-6 to PMN adherence to laminin when used alone because demonstration of VLA-dependent adherence requires that the CD11/CD18 be at least partially inhibited under the conditions used in this assay.
Fig 5. (A) Two-dimensional gel electrophoresis of PMN and platelet antigens recognized by the anti-α MoAb GoH3. (B) Two-dimensional gel electrophoresis of PMN and platelet antigens recognized by anti-β, MoAb 13. R, reduced (top figures); NR, nonreduced (bottom figures).
when CD11/CD18-dependent adhesion is maximally expressed, as it is under the conditions of this assay.

It has previously been shown that anti-β2 MoAbs, including IB4, completely reverse CD11/CD18-dependent PMN adherence to a number of other protein surfaces besides laminin. Thus, it is unusual for MoAb IB4 to be unable to completely inhibit CD11/CD18-dependent adhesion to laminin. The additive inhibition of adherence seen when IB4 and 60.1 are used together suggests that laminin might interact with several sites within the CD11/CD18 heterodimers. This explanation suggests, however, that laminin is a ligand for CD11/CD18, a hypothesis supported by the inhibition of PMN adherence to laminin by anti-CD11/CD18 MoAbs and by the decreased adherence of CD11/CD18-deficient PMNs to laminin. These results must be interpreted cautiously in the absence of more direct evidence of CD11/CD18 binding to laminin. Published studies showing that stimulated PMNs treated with MoAbs directed against the CD11/CD18 or congenitally lacking the CD11/CD18 adhere poorly to a large variety of surfaces suggest that the PMN CD11/CD18 receptors are promiscuous in their specificity and bind to a large variety of ligands. An alternative hypothesis, however, is that PMN CD11/CD18 are not promiscuous receptors but rather play a more general role in cell adhesion. If so, identification of PMN receptors that bind specifically and selectively to macromolecules may enhance our understanding of PMN behavior in the extravascular space.

The results of this study further confirm other reports showing that human PMNs possess both β1 and β2 integrin receptors, a property that PMNs share with lymphocytes and monocytes. The physiologic importance of the β2 integrins for normal leukocyte function can be inferred from the poor leukocyte adhesion and recurrent infections seen in patients with CD11/CD18 deficiency. A genetic defect clarifying the function of the leukocyte β integrins has not been described, but it has been postulated that the leukocyte β integrins mediate adherence of leukocytes to extracellular matrix, or that interaction of these receptors with their connective tissue ligands modulates leukocyte function. Exposure of PMNs to a variety of extracellular matrix molecules, including laminin, has been shown to influence their behavior in vitro. It is interesting to note that Gresham et al have recently shown that exposure of PMNs to laminin in vitro enhances PMN phagocytosis of IgG-coated particles, an effect similar to that of laminin on macrophage phagocytosis. This effect appears to be mediated through a β integrin because an MoAb directed against β, abolishes laminin’s effect (H.D. Gresham, personal communication, November 7, 1990). Specific recognition of basement membrane laminin by PMN VLA-6 may alter PMN function, or may be involved in adherence-dependent events such as directed migration through subendothelial basement membrane.

ACKNOWLEDGMENT

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CD11/CD18-independent neutrophil adherence to laminin is mediated by the integrin VLA-6

JF Bohnsack