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Cell Biology

Immunologic relationship between platelet membrane glycoprotein GPIIb/IIIa and cell surface molecules expressed by a variety of cells*

(adhesion receptors/membrane proteins/cytoadhesins)

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ABSTRACT **A polyclonal antiserum to platelet membrane glycoprotein GPIIb/IIIa was used to detect antigenically related molecules on a diverse panel of human cells. Umbilical vein endothelial cells, erythroleukemic HEL cells, and diploid fetal lung GM1380 fibroblasts expressed GPIIb/IIIa-related molecules, as judged by immunofluorescence and immunoprecipitation of surface-labeled proteins. The GPIIb and GPIIIa subunits were both present and were of similar molecular weight in these cell types. These molecules were synthetic products of the cells, as shown by immunoprecipitation of intrinsically labeled proteins. Promyeloid U937 cells could be induced by 4β-phorbol 12-myristate 13-acetate to synthesize and express GPIIb/IIIa-related molecules on their cell surface. The GPIIb/IIIa-related molecules were not precisely identical in the various cell types, based on slight differences in electrophoretic mobility and their failure to react with monoclonal antibodies specific for each subunit of platelet GPIIb/IIIa. These results suggest the existence of a widely distributed family of GPIIb/IIIa-related molecules. This family of "cytoadhesins" may share a common function in cellular adhesive reactions.**

The capacity of cells to recognize and adhere to elements of their surroundings plays a critical role in a wide variety of biological processes, including organ development, immune recognition, phagocytosis, and cellular aggregation. The interaction of specialized extracellular adhesive proteins with specific cell surface receptors is a basic mechanism underlying cellular adhesion. This general mechanism clearly governs the capacity of blood platelets to perform their hemostatic functions. At sites of blood vessel injury, platelets attach, spread, and aggregate to form a hemostatic plug. As a result of extensive investigations, a group of proteins that mediate platelet adhesive reactions has been identified and their cellular binding sites have been characterized. Platelet agonists such as thrombin can regulate the availability of the receptors for the adhesive proteins (reviewed in refs. 1 and 2).

Fibrinogen, fibronectin, and von Willebrand factor are members of a platelet adhesive-protein family. These large glycoproteins have internal symmetry, and each contains an Arg-Gly-Asp sequence (3, 4). This sequence, identified as a cell attachment site within fibronectin (5), may function as a general recognition site for cell adhesion to a variety of proteins (3). In support of this concept, the binding of fibrinogen, fibronectin, and von Willebrand factor to their thrombin-inducible platelet receptors is inhibited by Arg-Gly-Asp-containing peptides (6), and this effect is paralleled by an inhibition of platelet attachment and aggregation (6–9). Amino acid substitutions within the Arg-Gly-Asp sequence have the same effect on platelet and fibroblast adhesive reactions (6–10), suggesting that a common mechanism may be involved in the adhesion of both cell types.

Platelets from thrombasthenic patients exhibit deficits in the binding of fibrinogen, fibronectin, and von Willebrand factor (11–13). The membrane protein generally deficient on thrombasthenic platelets is glycoprotein GPIIb/IIIa (14). Additional evidence implicating GPIIb/IIIa as receptors for the adhesive proteins includes the capacity of purified GPIIb/IIIa in liposomes to bind fibrinogen and fibronectin (15, 16) and the photoaffinity crosslinking of fibrinogen and fibronectin to GPIIb/IIIa (17–19). GPIIb/IIIa exists in platelets as a noncovalent heterodimer comprised of a GPIIb subunit of ≈130 kDa and a GPIIIa subunit of ≈95 kDa (20). Recently, direct demonstration that GPIIb/IIIa is an Arg-Gly-Asp receptor has been provided, as this protein is selectively bound to an Arg-Gly-Asp affinity column (21). This approach has been previously utilized by Pytela *et al.* (22) to purify a vitronectin receptor from other cells, which is also comprised of nonidentical subunits with molecular masses very similar to those of GPIIb and GPIIIa. A fibronectin receptor isolated from osteosarcoma cells also appears to be comprised of a complex of 140-kDa proteins (23), and antibodies that inhibit the adhesion of chicken myoblasts and fibroblasts have been used to immunopurify noncovalent complexes with subunits of similar size (24–28). These observations raise the possibility that GPIIb/IIIa is a member of a family of structurally related membrane proteins involved in mediating cellular adhesive reactions. To test this hypothesis, we have performed an immunologic search for molecules antigenically related to GPIIb/IIIa in a variety of cells. While previous studies have shown that endothelial cells, which share a number of constituents with platelets, have GPIIb/IIIa-like molecules (29, 30), our study demonstrates that very diverse human cell types also express related species, establishing the existence of a family of these molecules.

METHODS

Preparation and Characterization of Anti-GPIIb/IIIa. GPIIb/IIIa was purified from outdated human platelet concentrates by a modification of the method of Jennings and Phillips (20). In brief, platelet membranes were solubilized in 200 mM *n*-octyl glucoside and separated from other membrane proteins by gel filtration on an Ultrogel AcA 34 column.

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Abbreviation: PMA, 4β-phorbol 12-myristate 13-acetate.

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Only two bands were detected in such preparations by $NaDodSO_4$/PAGE (see Fig. 1, lane 1), and these reacted with monoclonal antibodies specific for GPIIb (PMI-1) and GPIIIa (22C4). Rabbit anti-GPIIb/IIIa was elicited by injecting 100 μg of the purified protein in complete Freund's adjuvant. Booster injections, given at multiple intradermal sites, were administered in incomplete Freund's adjuvant on a weekly schedule for 3 weeks and then biweekly for an additional 3 months.

Specificity of the antiserum for GPIIb/IIIa was established by immunoblotting and immunoradiometric assays. Immunoblots were performed on the proteins electrophoretically transferred to nitrocellulose paper (31), using peroxidase-conjugated goat anti-mouse IgG (Cappel Laboratories, Cochranville, PA) for visualization. In the immunoradiometric analyses, GPIIb/IIIa (2.5 μg/ml) or citrate-treated, platelet-free plasma (50 μl) was used to coat the wells of polyvinyl chloride microtiter plates (Falcon, Oxnard, CA). After the plates were washed and postcoated with 3% gelatin, serial dilutions of the rabbit anti-GPIIb/IIIa were added for 1 hr at 37°C, followed by 50 ng of radioiodinated goat anti-rabbit IgG (200,000 cpm per well) for 1 hr at 37°C. The titer of the antibody was >1:100,000 on the GPIIb/IIIa plates compared to ≤1:10 on plasma-coated plates. Plasma failed to inhibit the reaction of the antiserum with GPIIb/IIIa, whereas purified GPIIb/IIIa completely inhibited binding.

Two monoclonal antibodies were used in this study. PMI-1 is GPIIb-specific (32), whereas 22C4 is GPIIIa-specific, based on immunoblotting and its decreased reactivity with thrombasthenic platelets. Both antibodies were purified from ascitic fluid on protein A-Sepharose (Bio-Rad). Binding of the ^{125}I-labeled antibodies to platelets and U937 cells was assessed by adding them at 0.5 μM, a saturating concentration for platelets, to the cells suspended at 2×10^7 per ml in Tyrode's buffer, pH 7.4/2% albumin/5 mM EDTA. After 30 min at 37°C, bound ligand was separated from free ligand by centrifugation through 20% sucrose (33). Specific binding was measured in the presence of a 50-fold excess of nonlabeled antibody.

Cell Isolation and Cell Lines. Human platelets were isolated by differential centrifugation followed by gel filtration (33). Human endothelial cells were isolated from umbilical veins as described (34), and only primary cultures were used. The human erythroblastoid cell line HEL (35) was from T. Papayannopoulou (University of Washington, Seattle, WA), the human diploid fetal fibroblast line GM1380 was from the Human Genetic Mutant Cell Repository (Camden, NJ), and the human promyeloid leukemic cell line U937 (36) was from H. Koren (Duke University). 4β-Phorbol 12-myristate 13-acetate (PMA) at 100 nM was used to stimulate differentiation of the U937 cells.

Radiolabeling and Immunoprecipitation. Cells (10^7–10^8) were surface-radioiodinated with lactoperoxidase by an adaption of the procedure of Skubitz *et al.* (37). Adherent cells (GM1380 and endothelial cells), grown to confluence in 75-cm^2 tissue culture flasks, were washed three times with cold phosphate-buffered saline (PBS: 0.01 M phosphate/0.15 M NaCl, pH 7.3) and then 5 ml of cold PBS was added. Nonadherent cells (platelets, U937, and HEL) were washed twice by centrifugation in cold PBS and then resuspended in 1–2 ml of cold PBS. Lactoperoxidase (200 μg) was added, followed by 2–3 mCi of carrier-free $Na^{125}I$ (16 mCi/μg, Amersham; 1 Ci = 37 GBq). H_2O_2 was then added in two 20-μl additions from a 0.06% stock solution at 5-min intervals at 4°C. The reaction was stopped by addition of 200 μg of tyrosine. The cells were washed five times with cold PBS and lysed in 0.5% Triton X-100 containing EDTA (10 mM), benzamidine (10 μg/ml), and Trasylol (100 units/ml).

For intrinsic labeling, cells were placed in 1–3 ml of methionine-free Dulbecco's modified Eagle's medium (DMEM), and 300–500 μCi of [^{35}S]methionine (1175 Ci/mmol, Amersham) was added. Cells were harvested after 6 hr by washing 3–5 times in DMEM supplemented with 1 mM methionine, and then lysis buffer was added. For pulse–chase experiments, the cells were treated as above and then placed in their original growth medium.

Fixed *Staphylococcus aureus* cells (Pansorbin, Behring Diagnostics, La Jolla, CA) were used for immunoprecipitation in a buffer [IPB: 0.02 M Tris Cl, pH 7.4/0.15 M NaCl/0.01 M EDTA/10 mM benzamidine·HCl/soybean trypsin inhibitor (10 μg/ml)/0.2 mM phenylmethylsulfonyl fluoride/1% (vol/vol) Triton X-100/0.05% Tween 20/0.02% NaN_3/Trasylol (5 units/ml)]. Lysates were precleared three times by adding 15 μl of heat-inactivated normal rabbit serum per ml of lysate, incubating the sample for 30 min at 22°C, adding 0.1 volume of Pansorbin, and centrifuging for 1 min in a Beckman Microfuge B. This process was followed by an additional clearing with Pansorbin alone. The cleared lysates were then supplemented with 1% bovine serum albumin and 250 μl of IPB containing 4 μl of either anti-GPIIb/IIIa or normal rabbit serum. Samples were incubated overnight at 4°C, and Pansorbin was then added. After 1 hr at 22°C, samples were centrifuged and the recovered immunoprecipitates were washed twice with IPB, once with 0.5 M LiCl, and once again with IPB. The immune complexes were solubilized by heating for 3 min at 100°C in 2% $NaDodSO_4$. Samples were then centrifuged and analyzed by electrophoresis in 6% polyacrylamide slab gels in the buffer system of Laemmli (38). For sample reduction, 5% 2-mercaptoethanol was added; *N*-ethylmaleimide was added to nonreduced samples. Gels were dried and autoradiograms were developed with Kodak X-Omat AR film. Gels containing [^{35}S]methionine were treated in 1 mM sodium salicylate prior to autoradiography. Molecular weights were estimated on the basis of electrophoretic mobility relative to standards obtained either from Pharmacia or from New England Nuclear (^{14}C-labeled protein standards).

Immunofluorescence. Adherent cells were grown on coverslips and fixed in 2% paraformaldehyde. Nonadherent cells were fixed in suspension and permitted to attach to poly(L-lysine)-coated coverslips. The cells were incubated for 20 min with a 1:25 dilution of the rabbit anti-GPIIb/IIIa, rinsed in PBS, and stained for 20 min with rhodamine-labeled $F(ab')_2$ fragments of goat anti-rabbit immunoglobulin (Cappel Laboratories). Blocking controls were performed by incubating the anti-GPIIb/IIIa with GPIIb/IIIa (50 μg/ml) for 20 min prior to staining. Cells were viewed and photographed as described (39).

RESULTS

Antiserum to GPIIb/IIIa was elicited in rabbits, and its specificity was characterized in immunoradiometric assays (see *Methods*) and by immunoblotting analysis (Fig. 1). The antiserum recognized both GPIIb and GPIIIa and showed no reactivity with other platelet proteins. Purified GPIIb/IIIa neutralized the reactivity of the antibody.

The capacity of this antiserum to react with cell surface proteins of other cells was assessed. The human erythroleukemic cell line HEL, a primary passage culture of human umbilical vein endothelial cells, and the diploid fetal fibroblast cell line GM1380 were subjected to lactoperoxidase-catalyzed surface radioiodination, and immunoprecipitates obtained with the GPIIb/IIIa antiserum were analyzed by $NaDodSO_4$/PAGE (Fig. 2). Specific bands were observed in the immunoprecipitates of all three cell types. For platelets, the immunoprecipitable radioactivity represented approximately 10% of the labeled proteins (trichloroacetic acid-precipitable radioactivity), as compared to ≈1% for the other cell types. When nonimmune rabbit serum was substituted

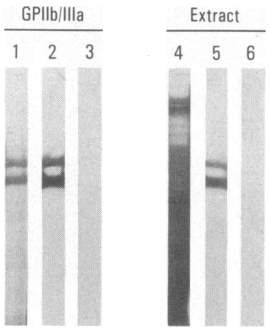

FIG. 1. Characterization of the polyclonal anti-GPIIb/IIIa by immunoblotting analysis. Purified GPIIb/IIIa (5 μg) and a detergent-solubilized extract of 10^7 washed human platelets were subjected to $NaDodSO_4$/7% PAGE under nonreducing conditions and then electrophoretically transferred to nitrocellulose. Lanes 1 and 4: amido black staining of the transfers. Lanes 2 and 5: blots obtained with a 1:100 dilution of the anti-GPIIb/IIIa and developed with peroxidase-conjugated anti-rabbit IgG. Lanes 3 and 6: same as lanes 2 and 5 except that the anti-GPIIb/IIIa was preabsorbed with purified GPIIb/IIIa (50 μg/ml).

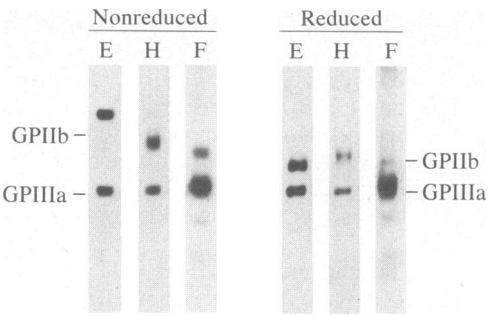

FIG. 2. Immunoprecipitates of GPIIb/IIIa-related molecules from human umbilical vein endothelial cells (E), HEL cells (H), and GM1380 fibroblasts (F). Cells were subjected to lactoperoxidase-catalyzed surface radioiodination, and the cell lysates were subjected to immunoprecipitation with polyclonal anti-GPIIb/IIIa. Immunoprecipitates were subjected to $NaDodSO_4$/6% PAGE under nonreducing (*Left*) or reducing (*Right*) conditions. Autoradiograms of the dried gels are shown. Controls in which nonimmune rabbit serum was substituted for the anti-GPIIb/IIIa or the antiserum was preabsorbed with purified GPIIb/IIIa were routinely analyzed, and no bands were detected. Positions of platelet GPIIb and GPIIIa were determined from the migration of the purified proteins. Gels shown are composited from several gel runs, so that precise mobilities cannot be compared. Molecular weights estimated from several such gels are summarized in Table 1.

for the GPIIb/IIIa antiserum, these bands were not detected even when the autoradiographic exposure time was extended 2- to 3-fold. In addition, development of the immunoprecipitates from each cell line could be blocked by addition of purified platelet GPIIb/IIIa to the antiserum. For all three cell types, two major radioactive bands predominated under both reducing and nonreducing conditions. These bands were of generally similar mobilities to one another and to platelet GPIIb and GPIIIa subunits. The molecular weights of the β subunits (band of greater mobility) were similar under nonreducing conditions and decreased slightly for all cells upon reduction (Table 1). The molecular weights of the α subunits (band of lesser mobility) were also very similar to one another. Reduction resulted in a decrease of ≈10,000 in apparent molecular weight, except for the GM1380 cells. Although these molecular weight estimates clearly indicate that the two sets of bands from the cell types migrated similarly, when immunoprecipitates from different cells were electrophoresed in the same gel, precise comigration of the bands was not observed. In such analyses, the two bands from the fibroblasts and endothelial cells were of slightly lower mobility than platelet GPIIb and GPIIIa.

Immunofluorescence indicated that virtually all HEL, GM1380, and endothelial cells within a culture expressed the GPIIb/IIIa-related antigens. Representative microscopic fields are shown in Fig. 3. HEL cells exhibited a rim of fluorescence staining, circumscribing the entire cell. Endothelial and GM1380 cells also exhibited surface staining, but inhomogeneities were noted. The specificity of the immunofluorescence reactions was indicated by the capacity of platelet GPIIb/IIIa to block the staining of each cell type.

Studies were performed to establish that the GPIIb/IIIa-related molecules were synthesized by these cells. The cells were pulsed for 6 hr with [^{35}S]methionine and then chased for 24 hr with nonlabeled methionine, and the cell lysates were immunoprecipitated with the GPIIb/IIIa antiserum. These immunoprecipitates and the corresponding controls obtained with nonimmune rabbit serum were subjected to $NaDodSO_4$/PAGE and autoradiography (Fig. 4). Two major polypeptides were specifically immunoprecipitated. The molecular weights of these were similar to those estimated for surface-expressed forms of the molecules. Although detailed studies of cellular processing were not performed, initial studies with endothelial cells were consistent with maturation of the GPIIb/IIIa-related molecules. Following a 6-hr pulse, four bands were detected in the immunoprecipitate (Fig. 4), and this pattern simplified to the two major bands after a 24-hr chase. This time-dependent change may reflect processing of precursor forms of the glycoproteins, such as conversion of a single-chain GPIIb-like molecule to a two-chain molecule [as shown in cell-free synthesis with mRNA derived from HEL cells (40)], changes in glycosylation, and/or synthesis of multiple forms of the glycoproteins with different rates of metabolism.

The U937 cell line provided an excellent control for the specificity of the described analyses, as the synthesis of the GPIIb/IIIa-related molecules in these cells could be regulated. Noninduced U937 cells were negative for GPIIb/IIIa by immunofluorescence (Fig. 5*A*). In contrast, when the cells were stimulated for 24 hr with 0.1 μM PMA, immunofluorescence staining was observed. All cells within the culture were positive, with a pattern consistent with surface expression, and this reactivity was blocked by purified platelet GPIIb/IIIa. In a pulse–chase experiment with

Table 1. Estimated molecular weights of the GPIIb/IIIa-related molecules from various cell types

Cell	Nonreduced		Reduced	
	α subunit	β subunit	α subunit	β subunit
HEL	139,300 ± 7,300	93,500 ± 2,400	132,700 ± 6,400	107,800 ± 4,800
Endothelial	143,500 ± 6,500	98,100 ± 5,400	134,800 ± 11,400	104,200 ± 8,800
GM1380	144,700 ± 1,700	96,800 ± 7,500	132,800 ± 5,600	99,300 ± 6,500
Platelet	139,000 ± 800	94,300 ± 6,800	129,000 ± 6,800	103,500 ± 8,300

Molecular weights were estimated from $NaDodSO_4$/PAGE of the immunoprecipitates obtained with the polyclonal anti-GPIIb/IIIa. Values shown are means ± SD from at least six separate immunoprecipitations from each cell type.

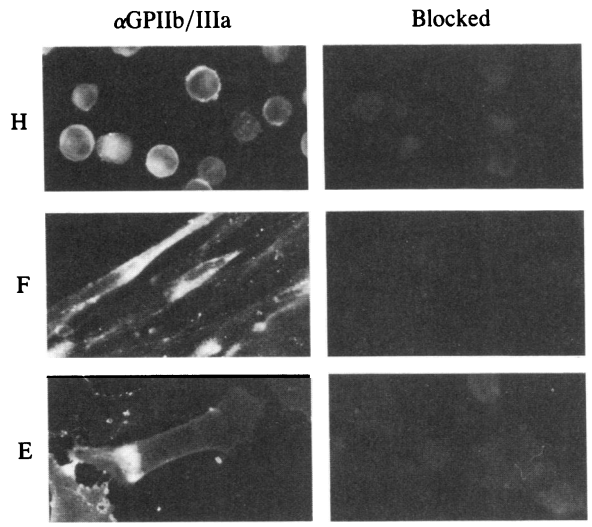

FIG. 3. Immunofluorescence staining of HEL cells (H), GM1380 fibroblasts (F), and umbilical vein endothelial cells (E) with polyclonal anti-GPIIb/IIIa. Paraformaldehyde-fixed cells were incubated with a 1:25 dilution of rabbit anti-GPIIb/IIIa (αGPIIb/IIIa) and then stained with rhodamine-labeled $F(ab')_2$ fragments of goat anti-rabbit immunoglobulin. Blocked control of each cell line was developed by preabsorbing the anti-GPIIb/IIIa with purified platelet GPIIb/IIIa (50 μg/ml).

[^{35}S]methionine, specific immunoprecipitates were obtained from the PMA-induced but not the noninduced U937 cells (Fig. 5*B*). The immunoprecipitate from the PMA-induced cells showed two major bands at estimated molecular weights of 133,000 and 103,000 (reducing conditions). With extended exposure of the autoradiogram of the gel of the noninduced U937 cells, only faint bands at these positions were detected.

The relationship between the GPIIb/IIIa-related species on induced U937 cells and platelets was further examined with monoclonal antibodies to platelet GPIIb (PMI-1) and GPIIIa (22C4). Under conditions where 38,600 ± 3,200 molecules of PMI-1 and 45,800 ± 1,900 molecules of 22C4 were specifically bound per platelet [values consistent with the reported number of copies of GPIIb and GPIIIa per platelet (41)], no specific binding of either monoclonal antibody to noninduced or PMA-induced U937 cells was detected. Thus, the GPIIb/IIIa-related molecules expressed on the surface of PMA-induced U937 cells are either not accessible to or not reactive with these antibodies to platelet GPIIb and GPIIIa.

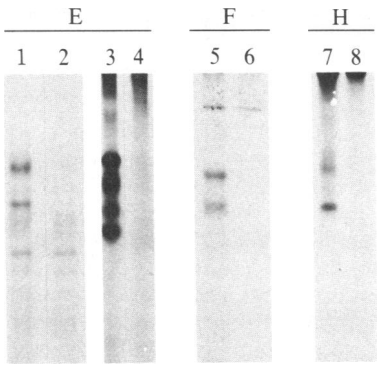

FIG. 4. Immunoprecipitates from umbilical vein endothelial cells (E), GM1380 fibroblasts (F), and HEL cells (H) intrinsically labeled with [^{35}S]methionine. Cells were incubated with [^{35}S]methionine for 6 hr and then processed (lanes 3 and 4) or were chased with nonlabeled methionine for an additional 24 hr prior to immunoprecipitation. Immunoprecipitates were subjected to $NaDodSO_4$/6% PAGE under nonreducing conditions; autoradiograms of the dried gels are shown. Lanes 1, 3, 5, and 7: immunoprecipitates obtained with anti-GPIIb/IIIa. Lanes 2, 4, 6, and 8: immunoprecipitates obtained with nonimmune serum.

DISCUSSION

In this study, we have shown that four different cell types synthesize and express on their surface molecules that are immunologically related to platelet GPIIb/IIIa. HEL cells have been previously shown (40, 42) to contain and synthesize platelet constituents, including GPIIb/IIIa. The presence of GPIIb/IIIa-related molecules on endothelial cells has recently been demonstrated (29, 30), consistent with the many shared specialized proteins of platelets and endothelial cells. The present study demonstrates the presence of GPIIb/IIIa-related molecules on fibroblasts (GM1380 cells) and the promyeloid (U937) cells. This indicates the existence of a broadly distributed family of GPIIb/IIIa-related molecules. In addition to the antigenic relationship between these molecules defined by the polyclonal anti-GPIIb/IIIa, similarities in several aspects of their behavior were observed. First, these are cell surface molecules, as shown by immunofluorescence and surface-iodination studies. Second, the estimated molecular weights of the GPIIb/IIIa-related molecules are very similar to one another. Third, the mobility of the β subunits corresponding to platelet GPIIIa increased slightly upon sample reduction. The latter observation has been interpreted to indicate the existence of intrachain disulfide bridges in platelet GPIIIa (43), and this may be a

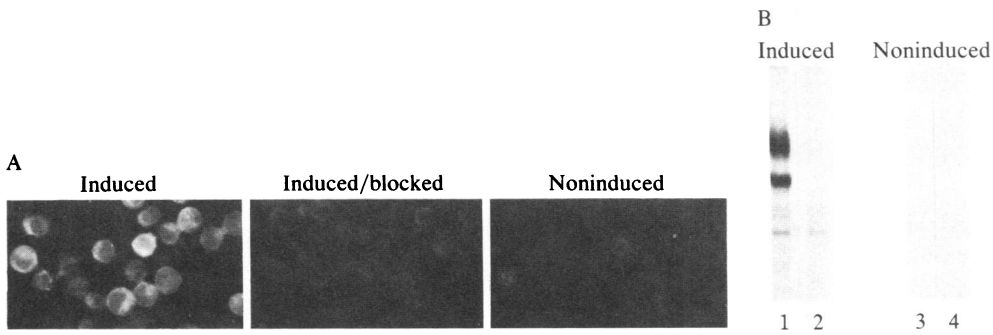

FIG. 5. Expression of GPIIb/IIIa-like molecules by noninduced and induced (0.1 μM PMA for 24 hr) U937 cells. (*A*) Immunofluorescence staining was performed as described for Fig. 3, using the rabbit anti-GPIIb/IIIa. As a control, PMA-induced cells were stained using antiserum blocked by preabsorption with purified platelet GPIIb/IIIa. (*B*) $NaDodSO_4$/PAGE analyses of the immunoprecipitates obtained with anti-GPIIb/IIIa (lanes 1 and 3) or with nonimmune rabbit serum (lanes 2 and 4). Analyses were performed as for Fig. 4, using a 6-hr pulse and 24-hr chase. Extracts from induced and noninduced U937 cells contained similar quantities of [^{35}S]methionine incorporated into 15% trichloroacetic acid-precipitable protein.

common feature of these β subunits. Nevertheless, the lack of precise comigration of the immunoprecipitated bands from the various cells and the failure of monoclonal antibodies PMI-1 and 22C4 to react with the U937 cells suggests that these related molecules are not identical.

The induction of GPIIb/IIIa-related molecules on PMA-stimulated U937 cells merits comment, as these cells exhibit certain monocyte-like properties. The presence of GPIIb/IIIa on monocytes has been extensively debated (44–46). Our data indicate that the state of differentiation and the GPIIb/IIIa antibodies utilized may determine the capacity to detect related molecules on cells of the monocyte lineage.

GPIIb/IIIa is implicated in the adhesive reaction of platelets. Proteins of similar molecular weight properties have been isolated as receptors for the adhesive glycoproteins vitronectin (22) and fibronectin (23), from tissues and cultured cells. Indeed, the polyclonal GPIIb/IIIa antiserum utilized in this study crossreacts with isolated vitronectin receptor (M.H.G., E.F.P., M. D. Pierschbacher, and E. Ruoslahti, unpublished results). These receptors and platelet GPIIb/IIIa recognize Arg-Gly-Asp sequences (21–23). Arg-Gly-Asp-containing peptides affect a diverse array of adhesive reactions, including platelet aggregation (6–9), attachment of cells to substrata (3, 10, 47), migration and attachment reactions of *Dictyostelium discoideum* (48), and gastrulation of amphibian embryos and migration of avian neural crest cells (49). Thus, the GPIIb/IIIa-related molecules may constitute a family of structurally and antigenically related adhesion receptors with a recognition specificity for Arg-Gly-Asp sequences. Consistent with this hypothesis is the existence of fibrinogen binding sites on fibroblasts (50) and endothelial cells (51) as well as platelets, although the role of the GPIIb/IIIa-related molecules in these interactions remains to be established. Bacterial surface molecules that mediate cell adhesion have been termed "adhesins" (52). It seems appropriate to designate this family of immunologically (and presumably structurally and functionally) related eukaryotic adhesion receptors "cytoadhesins" in recognition of their source and function. The breadth of the cytoadhesin family and its relationship to other adhesion receptors such as the cell-adhesion-molecule (CAM) family (53) and the laminin receptor (28) can ultimately be resolved at the primary structural level.

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