Journal of Cellular Biochemistry 37:107-117 (1988)
Altered Glycosylation in Tumor Cells 155-165

Endogenous Lectins as Mediators of Tumor Cell Adhesion

Reuben Lotan and Avraham Raz

Department of Tumor Biology, The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77030 (R.L.); Michigan Cancer Foundation, Detroit, Michigan 48201 (A.R.)

Endogenous carbohydrate-binding proteins have been found in various normal tissues and cells. Although lectins with different sugar-binding specificities have been described, the most prevalent ones are those that bind β-galactosides. The ability of some normal and malignant cells to bind exogenous carbohydrate-containing ligands suggested that lectinlike activity is associated with the cell surface and that carbohydrate-binding proteins might mediate intercellular recognition and adhesion. We found that extracts of various cultured murine and human tumor cells exhibit a galactoside-inhibitable hemagglutinating activity. This activity was associated with two proteins of molecular weights of 34,000 and 14,500 daltons, which were purified by affinity chromatography by using immobilized asialofetuin. That these lectins are present on the cell surface was indicated by the binding of monoclonal antilectin antibodies to the surface of various tumor cells and by the immunoprecipitation of ^{125}I-labeled lectins from solubilized cell-surface iodinated cells by polyclonal antilectin antibodies. That these cell surface lectins are functional was demonstrated by the ability of the galactose-terminating asialofetuin to enhance cell aggregation and of asialofetuin glycopeptides to block this homotypic aggregation as well as to suppress cell attachment to substratum, and by the inhibition of both asialofetuin-induced cell aggregation and cell attachment to substratum by the binding of monoclonal antilectin antibodies to the cell surface. These findings implicate cell surface lectins as mediators of cell-cell and cell-substratum adhesion. Some of these cellular interactions might be important determinants of tumor cell growth and metastasis.

Key words: galactose-binding proteins, intercellular interactions

Carbohydrate-containing macromolecules have been implicated in cell recognition and adhesion. The intercellular adhesion of mouse teratoma cells has been attributed to cell surface carbohydrates [1], and it has been suggested that they may bind to specific cell surface glycosyltransferases [2]. Support for this contention has come from the demonstration that teratoma cells produce an adhesion factor that can induce cell aggregation which can be inhibited by galactose [3]. More recently it has been shown that calcium-dependent adhesion of the embryonal carcinoma cells is mediated by the inter-

Received May 21, 1987; accepted September 30, 1987.

action of a cell surface galactosyltransferase with a cell surface lactosaminoglycan substrate, apparently through binding to *N*-acetylglucosamine residues [4].

A purified fucosyltransferase from human milk immobilized on polystyrene plates enhanced the adhesion of cells by binding cell surface oligosaccharide acceptors. This adhesion could be inhibited by glycoproteins, glycolipids, or oligosaccharides containing the sugar sequence galactosyl-(β1–4)-*N*-acetylglucosamine, in agreement with the substrate specificity of the enzyme [5]. Coating of a plastic surface with glycosidases including sialidase and β-galactosidase also enhanced cell adhesion in a substrate-specific manner [6]; α-mannosidase has been found on the surface of hamster embryo fibroblasts and shown capable of mediating cell adhesion by binding high-mannose-type glycopeptides on adjacent cells [7].

The presence of carbohydrate-binding proteins on the surface of various cells has been indicated by less direct studies that have not characterized the proteins involved except for their sugar specificity [8–14]. For example, virally transformed fibroblasts (SV403T3) adhere to Sephadex beads derivatized with galactose but not to beads derivatized with glucose or *N*-acetylglucosamine [8]. The exposure of galactose residues on the surface of untransformed baby hamster kidney (BHK) fibroblasts [9] or transformed 16C rat dermal fibroblasts [10] by neuraminidase treatment increased intercellular adhesiveness. Glycopeptides isolated from the surface of the BHK cells inhibited cell aggregation, especially when the glycopeptides were pretreated with neuraminidase [11]. Likewise, preincubation with galactose oxidase destroyed aggregation inhibitory activity of the glycopeptides [11]. Ricin-resistant BHK cells that have decreased expression of galactose residues on their surface, compared with the cells from which they were selected, exhibited a concurrent decrease in intercellular adhesiveness [12]. Studies on the adhesion of liposomes containing various glycolipids to HeLa carcinoma cells demonstrated that glycolipids containing terminal galactose residues were the most active in promoting adhesion [13,14].

MEDIATION OF ADHESION OF NORMAL CELLS BY ENDOGENOUS LECTINS

Extracts of many different normal tissues or cells were found to contain hemagglutinating activity that could be inhibited by specific carbohydrates, mostly β-galactosides. It was concluded that the cells contain lectinlike molecules [15–21]. Although most of these lectins were cytoplasmic, some activity was associated with the cell surface [20,21]. The lectins were localized on the membrane by the use of labeled (radioactive, fluorescent, or electron-dense) glycoproteins or neoglycoproteins (e.g., glycosylated albumin) in conjunction with quantitation of binding, fluorescence microscopy, flow cytofluorometry, or electron microscopy [20–23].

Lectins have been purified from extracts of many tissues and cells by affinity chromatography by using immobilized monosaccharides, oligosaccharides, or glycoproteins [15–21]. A large group of lectins exhibiting specificity for galactosides has been characterized in various vertebrates [15–21]; however, lectins with specificities for other sugars have also been described [21,24,25]. The most prevalent forms of galactoside-specific lectins are those with M_rs of 14,000 and 29,000–34,000 [17–19,26].

The involvement of endogenous lectins in adhesion has been demonstrated in various types of cell. For example, it has been shown that lectin-2, which is produced by embryonic chick muscle cells, reacts with glycosaminoglycans, and it has been suggested that the lectin interacts with glycosaminoglycans associated with the cell surface

or with the extracellular matrix [27]. Chicken hepatocytes possess an *N*-acetylglucosamine-specific lectin [28] that mediates their adhesion to gels derivatized with this sugar as indicated by the ability of the free sugar or of antilectin antibodies to block this adhesion [29]. Likewise, the endogenous asialoglycoprotein-binding lectin of rat hepatocytes mediates the adhesion of hepatocytes to polystyrene culture dishes coated with desialylated ceruloplasmin [30]. A different galactoside-specific lectin, found in extraembryonic endoderm cells of chick embryo [31], was also localized, by indirect immunofluorescence utilizing antilectin antibodies, to extracellular footprints deposited on the substratum by detaching cells [32], implying that the lectins are involved in adhesion to the substratum. The purified lectin inhibited cell aggregation, as did pretreatment of the cells with β-galactosidase [33]. These results suggest that the lectin and cell surface galactose-containing glycoconjugates are complementary partners in the formation of adhesive bonds. A β-galactoside-specific lectin from rabbit bone marrow [34] was isolated by affinity chromatography on immobilized asialofetuin and shown to agglutinate rabbit erythroblasts. This agglutination could be inhibited not only by galactose-containing glycoconjugates but also by Fab fragments of antilectin antibodies, providing evidence that the lectin bridges directly between cell surface glycoconjugates [35]. A membrane-bound lectin purified from BHK cells [25,36] agglutinated these cells more readily than several ricin-resistant mutants, which express less galactose residues on their cell surface membrane. These results support a model of cell-cell adhesion involving interaction of surface lectins with carbohydrate sequences on the surface of neighboring cells [12].

Rat liver cells, including hepatocytes, Kupffer cells (macrophages), and endothelial cells, express membrane lectins specific for *N*-acetylgalactosamine and galactose [37,38]. These lectins mediate adhesion of desialylated erythrocytes or lymphocytes in vitro and presumably also in vivo [39].

The presence of lectinlike molecules on the surface of lymphocytes has been demonstrated by several methods [40–42], and it has been proposed that such lectins are involved in the recirculation of lymphocytes from the bloodstream into lymphoid organs by specific binding of the lymphocytes to endothelial cells in postcapillary venules [42,43]. Fucoidin, a sulfated polysaccharide containing primarily α1,3-linked L-fucose, markedly inhibits the adhesion of lymphocytes to high endothelial venule sections, presumably by binding to the lymphocytes [43]. Lymphocyte hemagglutinin was inhibited by several sulfated polysaccharides including fucoidin [44]. Studies in other laboratories demonstrated that pretreatment of mouse spleen cells with neoglycoproteins containing β-galactosides inhibited cell adhesion to microvenules [45].

CARBOHYDRATE-BINDING PROTEINS AND ENDOGENOUS LECTINS IN MALIGNANT CELLS AND THEIR INVOLVEMENT IN CELL ADHESION

The presence of a galactoside-specific hemagglutinating activity in neoplastic cells was first demonstrated in murine neuroblastoma cell extracts [15]. The presence in murine embryonal carcinoma cells of a carbohydrate-binding protein specific for mannose-containing glycoproteins was implied by the ability of such glycoproteins to inhibit rosette formation by rabbit erythrocytes on the teratocarcinoma cells and to inhibit the reaggregation of dispersed cells [46]. We initiated studies to explore whether endogenous lectins are present in different tumor cells [47].

The initial indications that many cultured tumor cells contain lectinlike molecules

on their surface were based on the ability of fetuin and especially its desialylated derivative—asialofetuin—to induce homotypic aggregation of the tumor cells in the absence of Ca^{2+} (Fig. 1A,D). Glycopeptides prepared from asialofetuin by pronase digestion did not cause aggregation but rather were effective inhibitors of aggregation induced by intact asialofetuin (Fig. 2A) [48]. These results suggested that the intact molecule, which is polyvalent in that it contains several oligosaccharide side chains [49,50], can serve as a bridge between lectin molecules present on the surface of adjacent cells. Direct binding of fluorescently labeled asialofetuin to the surface of tumor cells was demonstrated by fluorescence microscopy [47]. The aggregation-inducing capacity was not restricted to asialofetuin, as syngeneic mouse serum was also an effective inducer. Furthermore, B16 melanoma cells selected for reduced ability to aggregate in the presence of asialofetuin exhibited a concurrent reduction in their ability to aggregate in the presence of syngeneic mouse serum [51].

Asialofetuin contains several terminal nonreducing galactose residues that are masked by sialic acid residues in the native fetuin molecule [49,50]. Since asialofetuin was more potent than fetuin in the induction of aggregation of different tumor cells, we presumed that these cells expressed a galactoside-specific cell surface lectin [47]. Using procedures that have been established for the extraction and purification of endogenous lectins from normal tissue and cells [15,52], we have demonstrated that different murine and human tumor cells contain soluble, lectinlike activity detectable by hemagglutination assay and inhibitable by galactosides [47]. The lectins mediating this hemagglutinating activity were purified by affinity chromatography by using immobilized asialofetuin (Fig. 3, lane A). The purified material consisted of two polypeptides of M_r 14,500 and 34,000,

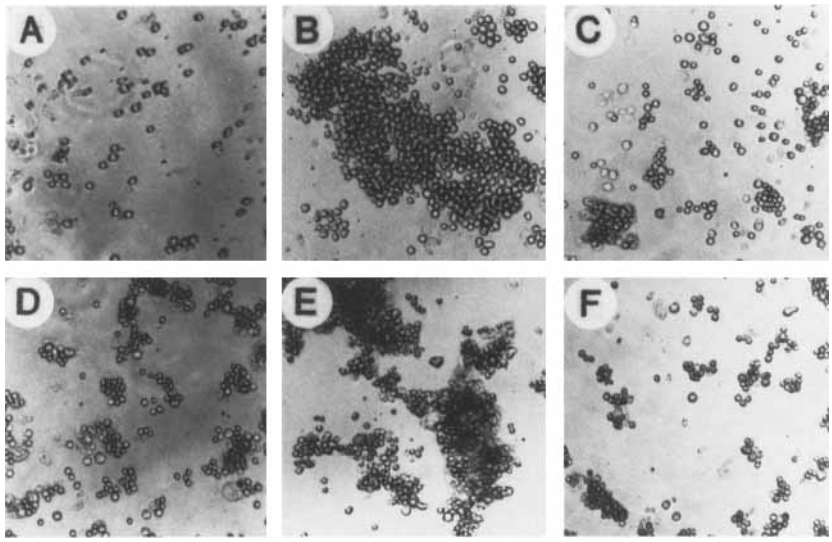

Fig. 1. Enhancement of homotypic tumor cell aggregation by asialofetuin and inhibition of this effect by antilectin mAbs. Murine B16-F1 (**A–C**) and UV-2237-IP3 cells (**D–F**) were allowed to aggregate spontaneously (A,D) in Ca^{2+}-free buffer or induced to aggregate with asialofetuin (25 μg/ml) alone (B,E) or in the presence of a 1:10 (vol:vol) dilution antilectin mAb 5D7 ascitic fluid (C,F). The cells were photographed by using a phase contrast microscope after a 1-hr agitation (80 rpm) at 37°C. Further details on the aggregation assay are given in Table I. (Reproduced from ref. 50 with permission.) × 45.

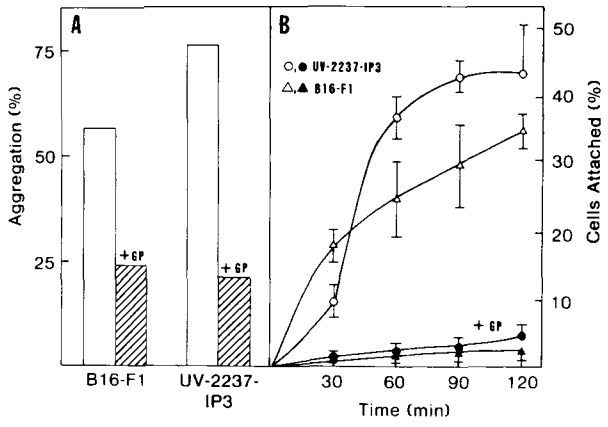

Fig. 2. Inhibition by asialofetuin glycopeptides of asialofetuin-induced homotypic cell aggregation (A) and cell-to-substratum attachment (B). In **A**, the tumor cells were induced to aggregate by the addition of asialofetuin alone (25 μg/ml, bars) or with asialofetuin glycopeptides (60 μg of hexose equivalents per ml, shaded bars) by agitation for 1 hr at 80 rpm at 37°C. The percentage of aggregation was determined as in Table I. In **B**, the tumor cells were labeled with $Na^{51}CrO_4$, suspended in Dulbecco's modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum, and allowed to adhere onto the bottom of wells of a 24-well tissue culture plastic cluster plate. After 30 min and at 30-min intervals thereafter, the medium and floating cells were removed by aspiration and the wells were washed gently with buffer to remove loosely attached cells. The firmly attached cells were then solubilized with 0.1 N NaOH, and the cell-associated radioactivity was counted. The percentage of attached cells was calculated by comparing the radioactivity measured in attached cells with the radioactivity in the cells that were originally introduced into each well (100%). *Points*, mean of triplicate determinations, *bars*, SE. (Reproduced from ref. 50 with permission.)

respectively. Such lectins were purified from murine fibrosarcoma UV-2237-IP3 [53], melanoma cell lines B16-F1, K-1735, and S91, and carcinoma HeLa-S3. The higher-M_r polypeptide could not be dissociated by boiling in 9 M urea and 2% sodium dodecylsulfate to the lower M_r polypeptide, and the peptide maps of the two polypeptides demonstrate only a partial overlap [53], suggesting that the M_r 34,000 lectin (L-34) is not a dimer form of the M_r 14,500 lectin (L-14.5). Separation by gel filtration of the two affinity-purified polypeptides revealed that both possess hemagglutinating capacity and thus both are lectins. Recently, two distinct genes coding for L-14.5 and L-34 have been cloned from the UV-2237-IP3 murine fibrosarcoma cells. RNA and DNA blot analysis indicated that the two lectins are products of two different genes [54].

Monoclonal antilectin antibodies (mAb) prepared against crude lectin extracts from the B16-F1 melanoma cells were capable of inhibiting lectin activity present in several different tumor cell extracts, including UV-2237-IP3 fibrosarcoma, RAW117P lymphosarcoma, HeLa-S3 carcinoma, and Hs939 melanoma cells [55]. One of the mAbs, designated 5D7, was shown by immunoblotting to bind specifically to purified lectins and to two comigrating polypeptides present in cell extracts (Fig. 3, lane B) [56]. The fact that the mAb recognizes both polypeptides indicates that they share at least one antigenic determinant. Likewise, the binding of the mAb to lectins of different tumor cell lines indicates that these lectins are similar not only in sugar specificity and electrophoretic migration but also in antigenic makeup [55,56]

These endogenous lectins have been localized, by indirect immunofluorescence

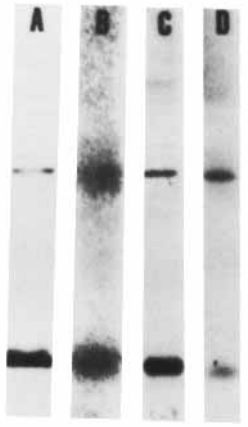

Fig. 3. Endogenous galactoside-specific lectins of murine UV-2237-IP3 fibrosarcoma cells. **A:** Autoradiogram of lectins isolated by affinity chromatography of extracts of [^{35}S]methionine-labeled cells with an immobilized asialofetuin column eluted with lactose. The purified lectins were separated by polyacrylamide gel electrophoresis in the presence of sodium dodecylsulfate (SDS-PAGE). **B:** Autoradiogram of an immunoblot of unlabeled affinity-purified lectins separated by SDS-PAGE, transferred onto nitrocellulose filter, and incubated sequentially with antilectin mAb 5D7 ascitic fluid diluted 1:50 and ^{125}I-labeled goat antimouse IgG. **C,D:** Autoradiograms of material immunoprecipitated by polyclonal antibodies prepared by immunizing rabbits with affinity-purified lectin of UV-2237-IP3 cells from solubilized [^{35}S]methionine-labeled cells (C) or cells labeled while intact by lactoperoxidase-catalyzed ^{125}I-iodination (D). The labeled cells were solubilized and incubated with antilectin antibodies. The antibody-antigen complexes were precipitated after binding to *Staphylococcus aureus* and analyzed by SDS-PAGE and autoradiography. The upper band had an apparent molecular weight of 34,000 daltons and the lower band 14,500 daltons compared to molecular weight standards analyzed on the same gels.

staining, at the surface of different viable cultured tumor cells and, after fixation and permeabilization, in intracellular pools (Fig. 4) [55]. The surface distribution was in the form of microclusters, suggesting that the membrane-associated lectin molecules were laterally mobile and subject to rearrangement by exogenous ligands (mAbs or glycoproteins). The intense labeling of intracellular lectin in vesicles suggests that most of the lectin is usually in the cytoplasm. Recently, a similar lectin localization was found in 3T3 fibroblasts by antibodies prepared against a M_r 35,000 endogenous lectin found in these cells [57].

The presence of both the L-14.5 and the L-34 lectins on the surface of UV-2237 fibrosarcoma cells was demonstrated by immunoprecipitation with polyclonal antilectin antibodies of extracts from cells surface labeled with ^{125}I by lactoperoxidase-catalyzed iodination (Fig. 3, lane D) [53].

Other investigators have demonstrated the presence of lectins or carbohydrate-binding proteins in cultured transformed and tumor cell lines as well as in tumors removed from experimental animals or human patients [21,22,46,58–78]. These lectins have been characterized to varying degrees. Endogenous lectins have been found in a large variety of transformed and tumor cell types, including rodent and human sarcomas [26,47,66,69,73,74,76], hepatomas [60,61,76,78], lung [65], mammary [69,75,76], and squamous cell carcinomas [76], ovarian and testicular teratocarcinomas [46,58,59,69,71,72], T- and B-human lymphoblastoid cells [64,68], hairy cell leukemia and chronic lymphocytic leukemia [68], Hodgkin's disease [77], murine leukemia [22], pituitary tumor

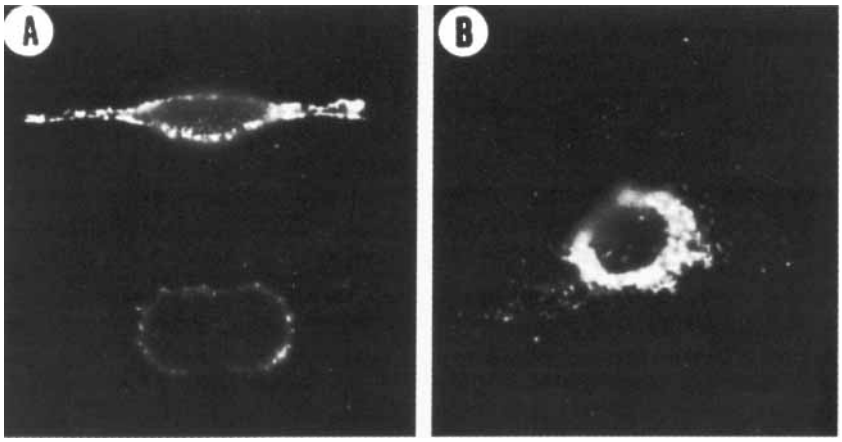

Fig. 4. Localization of endogenous lectins on the surface (**A**) and in the cytoplasmic compartment (**B**) of UV-2237-IP3 cells with indirect immunofluorescence staining. The cells were seeded on glass coverslips and after 24 hr the cells were incubated for 30 min at 4°C with antilectin mAb 5D7 (1:20 dilution of ascitic fluid) before (A) or after (B) fixation with 3.5% formaldehyde and permeabilization with 0.05% Nonidet P-40. Binding of mAb 5D7 was visualized by a further 30-min incubation at 4°C with rhodamine-conjugated goat antimouse IgG and observation and photography under a fluorescence microscope.

[62], and various other epithelial tumors [76]. These lectins have been detected by their agglutinating activity, by binding of fluoresceinated neoglycoproteins, by their purification by affinity chromatography on immobilized saccharides or glycoproteins, or by immunoblotting with antilectin antibodies. The M_r of different tumor lectins ranged between 13,000 and 140,000 as determined by polyacrylamide gel electrophoresis in the presence of sodium dodecylsulfate. Most cell types contained lectins of M_r 13,000–14,000, and 29,000–35,000 with different sugar specificities, including galactosides, mannose, mannan, fucose, fucoidin, heparin, and heparan sulfate. The location of most of these lectins has not been established. The presence of lectins at the cell surface was demonstrated in only a few of the above studies by rosetting with red blood cells, by binding of fluorescent glycosylated markers [22,65,66], binding of ^{125}I-asialoglycoprotein [60,61] or glycoprotein-containing micelles [64]. That different types of lectin may have different cellular compartments is indicated by differences in lectin extraction with salt or with detergents [69,76].

The participation of endogenous tumor cell surface lectins in intercellular adhesion was demonstrated by the formation of rosettes of fixed, trypsinized rabbit erythrocytes on cultured mouse teratocarcinoma cells and by homotypic aggregation of the tumor cells [46]. This cell-cell adhesion could be inhibited by the mannose-containing invertase or by the fucose-containing fucoidin. Likewise, the rosetting activity and the homotypic aggregation of an embryonal carcinoma cell line established from a primary human testicular tumor were inhibited by mannose, galactose, and glycoproteins containing one of these saccharides [71]. The homotypic aggregation of several human carcinoma cell lines exhibiting different cell surface carbohydrate-binding proteins, revealed by binding of fluorescent neoglycoproteins, was inhibited by specific saccharides as expected from their specificity for the glycoproteins [67]. We found that asialofetuin glycopeptides can inhibit the homotypic aggregation of murine melanoma and fibrosarcoma cells as well as their adhesion to solid substrates (Fig. 2). That these interactions are mediated via

TABLE I. Inhibition by Antilectin mAb 5D7 of Asialofetuin-Induced Homotypic Tumor Cell Aggregation*

Additive to aggregation medium	Aggregation (%)	
	B16-F1	UV-2237-IP3
None	0	0
ASF	41	38
mAb 5D7	9	12
ASF and mAb 5D7	13	8

*Cells were suspended at 1 × 10^6 cells/ml in Ca^{+2} and Mg^{+2}-free phosphate-buffered saline with and without asialofetuin (25 μg/ml), mAb 5D7 (a 1:10 dilution of ascitic fluid), or both. Aliquots containing 0.5 ml of the cell suspension were agitated at 80 rpm for 1 hr at 37°C and the number of single cells was determined. The percentage of aggregated cells was calculated according to the equation (1 − Nt/Nc) × 100 where Nt and Nc represent the number of single cells in the presence of a tested compound and in control buffer, respectively. (Reproduced from ref. 50, with permission).

the endogenous cell surface lectins was further implied by the ability of antilectin mAbs to inhibit homotypic aggregation induced by asialofetuin (Fig. 1C,F, Table I) and to inhibit the attachment of tumor cells to a solid substratum (Fig. 5).

The finding that many tumor cells, including metastatic cells, contain endogenous lectins on their surface raised the idea that these lectins might play a role in metastasis [47,79]. Quantitative analysis of cell surface lectins by flow cytometric analyses of

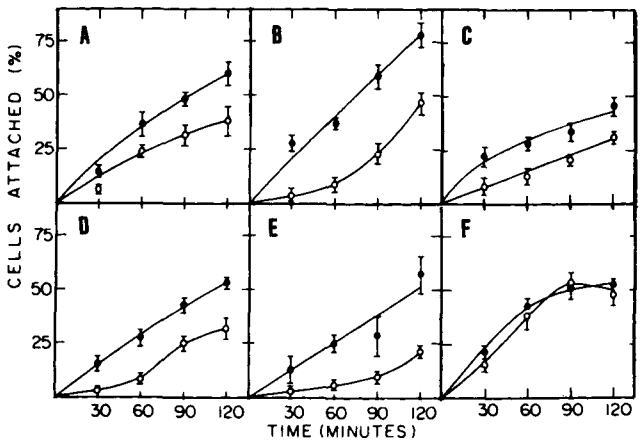

Fig. 5. Effect of preincubation with mAb 5D7 on attachment of untransformed and transformed cells to tissue culture plastic dishes. Cells were detached with 2 mM EDTA and washed with 10 ml phosphate-buffered saline. The cells were then suspended at 3 × 10^6 cells/ml in DMEM (without serum) containing 1% bovine serum albumin and radiolabeled for 2 hr at 37°C with 5 μCi of carrier-free $Na^{51}CrO_4$. At the end of incubation, the cell suspensions were washed extensively and suspended in DMEM containing 5% fetal bovine serum (heat inactivated) and supplement with 60 μg/ml Ig from syngeneic mouse serum (●) or mAb 5D7 from ascites fluid (○). The cell suspensions were immediately placed in microtiter plates at 10^4 cells/well and the plates were incubated at 23°C. After different time intervals the percentage of adherent cells was determined as described in Figure 2. **A:** Mouse B16-F1 cells. **B:** B16-F10 cells. **C:** SV40, polyoma-transformed 3T3 cells. **D:** UV-2237 clone 15. **E:** UV-2237-IP3. **F:** 3T3 fibroblasts. (Reproduced from ref. 50 with permission.)

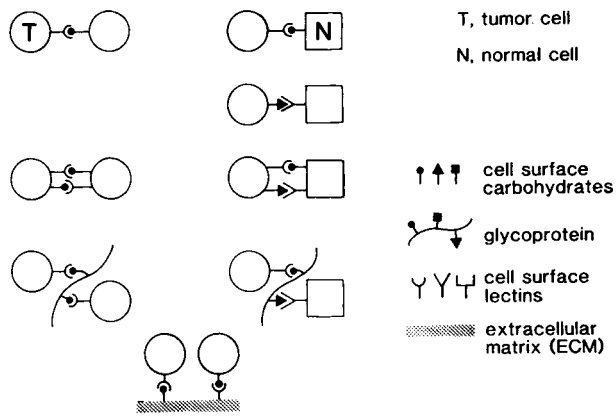

Fig. 6. A schematic representation of the mediation of cell adhesion by endogenous cell surface lectins.

antilectin antibody binding (indirect immunofluorescence) revealed that among related sublines, variants, or clones of murine B16, K-1735 melanoma, or UV-2237 fibrosarcoma, those exhibiting a higher metastatic potential express more lectin molecules on their surface [56]. Recently we found that preincubation of B16 melanoma or UV-2237 fibrosarcoma cells with the antilectin monoclonal antibodies inhibited lung metastasis after intravenous injection into the tail vein of syngeneic mice [48].

These results suggest that tumor cell surface lectins might mediate intercellular adhesive interactions that are relevant for metastasis.

Endogenous lectins might be involved in specific recognition and adhesion between tumor cells and host cells in vivo in at least two ways. On one hand, endogenous lectins present on the surface or certain normal host cells such as platelets, lymphocytes, macrophages, hepatocytes, endothelial cells, and some extracellular matrix (ECM) components might bind tumor cell surface glycoconjugates and promote heterotypic aggregation and adhesion of tumor cells to capillary walls and basal lamina. On the other hand, tumor cell surface lectins can recognize and bind complementary glycoconjugates on the surface of other tumor cells and mediate homotypic aggregation or bind to glycoconjugates on the surface of host cells to mediate heterotypic aggregation or attachment to endothelial cells or to ECM (Fig. 6).

ACKNOWLEDGMENTS

We thank Eleanor Felonia for excellent assistance in manuscript preparation. This research was supported by USPHS grant 7RO1-CA39422 awarded by the NCI, by M.D. Anderson Annual Campaign Funds (R.L.), and by the Minerva Foundation, FRG (A.R.)

REFERENCES

1. Oppenheimer SB, Edidin M, Orr CW, Roseman S: Proc Natl Acad Sci USA 63:1395, 1969.
2. Roseman S: Chem Phys Lipids 5:270, 1970.
3. Oppenheimer SB: Exp Cell Res 92:122, 1975.
4. Shur BD: Dev Biol 99:360, 1983.
5. Rauvala H, Prieels J-P, Finne J: Proc Natl Acad Sci USA 80:3991, 1983.

6. Rauvala H, Carter WG, Hakomori S-I: J Cell Biol 88:127, 1981.
7. Rauvala H, Hakomori S-I: J Cell Biol 88:149, 1981.
8. Chipowsky S, Lee YC, Roseman S: Proc Natl Acad Sci USA 70:2309, 1973.
9. Vicker MG, Edwards JG: J Cell Sci 10:759, 1972.
10. Lloyd CW, Cook GMW: J Cell Sci 15:575, 1974.
11. Vicker MG: J Cell Sci 21:161, 1976.
12. Edwards JG, Dysart JMcK, Hughes C: Nature 264:66, 1976.
13. Bussian RW, Wriston JC: Biochim Biophys Acta 471:336, 1977.
14. Huang RT: Nature 276:624, 1978.
15. Teichberg VI, Silman I, Beitsch DD, Resheff G: Proc Natl Acad Sci USA 72:1383, 1975.
16. Simpson DL, Thorne DR, Loh HH: Life Sci 22:727, 1978.
17. Harrison FL, Chesterton CJ: FEBS Lett 122:157, 1980.
18. Barondes S: Annu Rev Biochem 50:207, 1981.
19. Barondes SH: Science 23:1259, 1984.
20. Ashwell G, Harford J: Annu Rev Biochem 51:531, 1982.
21. Monsigny M, Kieda C, Roche AC: Biol Cell 47:95, 1983.
22. Monsigny M, Roche AC, Midoux P: Biol Cell 51:187, 1984.
23. Kolb H, Kolb-Bachofen V: Biochem Biophys Res Commun 85:678, 1978.
24. Rutherford NG, Cook GMW: FEBS Lett 136:105, 1981.
25. Dysart J, Edwards JE: FEBS Lett 75:96, 1977.
26. Crittenden SL, Roff CF, Wang JL: Mol Cell Biol 4:1252, 1982.
27. Ceri H, Shadle PJ, Kobiler D, Barondes SH: J Supramol Struct 11:61, 1979.
28. Kawasaki T, Ashwell G: J Biol Chem 252:6536, 1977.
29. Guarnaccia SP, Kuhlenschmidt MS, Slife CW, Schnaar RL: J Biol Chem 257:14293, 1982.
30. Hook M, Rubin K, Oldberg A, Obrink B, Vaheri A: Biochem Biophys Res Commun 79:726, 1977.
31. Cook GMW, Zalik SE, Milos N, Scott V: J Cell Sci 38:293, 1979.
32. Zalik SE, Milos N, Ledsham I: Cell Tissue Res 225:223, 1982.
33. Milos N, Zalik SE: Cell Differ 12:341, 1983.
34. Harrison FL, Chesterton CJ: Nature 286:502, 1980.
35. Godsave SF, Harrison FL, Chesterton CJ: J Supramol Struct Cell Biochem 17:223, 1981.
36. Stojanovic D, Hughes RC: Biol Cell 51:197, 1984.
37. Kolb H, Kolb-Bachofen V, Kolb HA: Cell Immunol 40:457, 1978.
38. Schlepper-Schafer J, Kolb-Bachofen V, Kolb H: Biochem J 186:827, 1980.
39. Kolb-Bachofen V, Schlepper-Schafer J, Roos P, Hulsmann D, Kolb H: Biol Cell 51:219, 1984.
40. Kieda CM, Roche AC, Delmotte F, Monsigny M: FEBS Lett 99:329, 1979.
41. Decker JM: Mol Immunol 17:803, 1980.
42. Kieda CM, Monsigny M, Waxdal MJ: In Bøg-Hansen TC, Spengler GA (eds): "Lectins: Biology, Biochemistry and Clinical Biochemistry." Berlin: de Gruyter, 1982, Vol 3, pp 427–433.
43. Stoolman LM, Rosen SD: J Cell Biol 96:722, 1983.
44. Parish CR, Rylatt DB, Snowden JM: J Cell Sci 67:145, 1984.
45. Kieda C, Monsigny M: In Parker JW, O'Brien RL (eds): "Intercellular Communication in Leucocyte Function." New York: John Wiley & Sons Ltd, 1983, pp 649.
46. Grabel LB, Rosen SD, Martin GR: Cell 17:477, 1979.
47. Raz A, Lotan R: Cancer Res 41:3642, 1981.
48. Meromsky L, Lotan R, Raz A: Cancer Res 46:5270, 1986.
49. Spiro RG, Bhoyroo VD: J Biol Chem 249:5704, 1974.
50. Baenziger JU, Fiete D: J Biol Chem 254:789, 1979.
51. Lotan R, Raz A: Cancer Res 43:2088, 1983.
52. Nowak TP, Kobiler D, Roel LE, Barondes SH: J Biol Chem 252:6026, 1977.
53. Raz A, Meromsky L, Zvibel I, Lotan R: Int J Cancer 39:353, 1987.
54. Raz A, Avivi A, Pazarini G, Carmi P: Exp Cell Res 173:109, 1987.
55. Raz A, Meromsky L, Carmi P, Karakash R, Lotan D, Lotan R: EMBO J 3:2979, 1984.
56. Raz A, Meromsky L, Lotan R: Cancer Res 46:3667, 1986.
57. Moutsatsos IK, Davis JM, Wang JL: J Cell Biol 102:477, 1986.
58. Grabel LB: Cell Differ 15:121, 1984.
59. Grabel LB, Singer MS, Martin GR, Rosen SD: FEBS Lett 183:228, 1985.
60. Schwartz AL, Fridovich SE, Knowles BB, Lodish HF: J Biol Chem 256:8878, 1981.

61. Schwartz AL, Rup D: J Biol Chem 258:11249, 1983.
62. Wieser R, Golecki JR, Brunner G: Biochim Biophys Acta 648:275, 1981.
63. Carrol SB, Ippolito LM, Dewolf WC: Biochem Biophys Res Commun 109:1353, 1982.
64. Apgar JR, Cresswel P: Eur J Immunol 12:570, 1982.
65. Roche AC, Barzilay M, Midoux P, Junqua S, Sharon N, Monsigny M: J Cell Biochem 22:131, 1983.
66. Jiang PH, Fournier FC, Galliot BR, Sarragne M, Chany C: J Biol Chem 258:12361, 1983.
67. Graupner GA, Vollmers HP, Birchmeier W, Gabius HJ, Cramer F: Hoppe Seylers Z Physiol Chem 365:992, 1984.
68. Carding SR, Thorpe SJ, Thorpe R, Feizi T: Biochem Biophys Res Commun 127:680, 1985.
69. Gabius HJ, Engelhardt R, Rehm S, Cramer F: J Natl Cancer Inst 73:1349, 1984.
70. Gabius HJ, Engelhardt R, Cramer F, Batge R, Nagel GA: Cancer Res 45:253, 1985.
71. Gabius HJ, Engelhardt R, Casper J, Reile D, Schumacher S, Schmoll JH, Graupner G, Cramer F: Tumour Biol 6:145, 1985.
72. Gabius HJ, Engelhardt R, Casper J, Schmoll HJ, Nagel GA, Cramer F: Tumor Biol 6:471, 1985.
73. Gabius HJ, Vehmeyer K, Engelhardt R, Nagel GA, Cramer F: Cell Tissue Res 241:9, 1985.
74. Gabius HJ, Engelhardt R, Sartoris DJ, Cramer F: Cancer Lett 31:139, 1986.
75. Gabius HJ, Engelhardt R, Rehm S, Deerberg F, Cramer F: Tumor Biol 7:71, 1986.
76. Gabius HJ, Engelhardt R, Rehm S, Barondes SH, Cramer F: Cancer J 1:19, 1986.
77. Paietta E, Stockert RJ, Morell AG, Diehl V, Wiernik PH: Proc Natl Acad Sci USA 83:3451, 1986.
78. Gitt MA, Barondes SH: Proct Natl Acad Sci USA 83:7603, 1986.
79. Raz A, Lotan R: In Galeotti T, Cittadini A, Neri G, Papa S (eds): "Membranes in Tumor Growth." Elsevier: Amsterdam, 1982, pp 213.