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# Galectin-3 Regulates the Adhesive Interaction Between Breast Carcinoma Cells and Elastin

**Josiah Ochieng,**[1]* **Paula Warfield,**[1] **Brenda Green-Jarvis,**[1] **and Ian Fentie**[2]

[1]Department of Biochemistry, Meharry Medical College, Nashville, Tennessee 37208
[2]Departments of and Anatomy and Physiology, Meharry Medical College, Nashville, Tennessee 37208

**Abstract** Galectin-3 is a beta-galactoside binding lectin whose precise physiological role is not yet defined. In the present studies, we questioned whether galectin-3 plays a role in the adhesion of breast carcinoma cells to elastin. The impetus for this analysis was the initial observation that the cellular receptor for elastin, the 67 kDa elastin/laminin protein may have galectin-like properties (Mecham et al. [1989] J. Biol. Chem. 264:16652–16657). We therefore analyzed the adhesion of breast carcinoma cells to microtiter wells coated with elastin under conditions which eliminate integrin participation in adhesion. The adhesion assay was done in the absence and presence of purified recombinant galectin-3. We hereby demonstrate that high concentrations of galectin-3 ligate breast carcinoma cells to microtiter wells coated with elastin. Galectin-3 also demonstrated a specific binding interaction with purified elastin in a dose and lactose dependent manner. Furthermore we demonstrated by immunoprecipitation that endogenous galectin-3 in breast carcinoma cells is associated with tropoelastin. Lastly, the breast carcinoma cells which expressed galectin-3 on their surface, demonstrated enhanced cellular proliferation on elastin compared to galectin-3 null expressing cells. These studies suggest that galectin-3 is capable of regulating the interactions between cells and elastin. J. Cell. Biochem. 75:505–514, 1999. 

**Key words:** galectin-3; elastin; ligation; breast; carcinoma

Whereas the precise physiological role of galectin-3 is still elusive, mounting evidence suggests its involvement in the regulation of cell-extracellular matrix interactions [Sato and Hughes, 1992; ochieng et al., 1992; Warfield et al., 1997; Kuwabara and Liu, 1996]. In breast epithelial cells, low expression of galectin-3 has been linked to low cloning and plating efficiencies while high expression improves the interaction of cells with different substrata [Makker et al., 1995; Warfield et al., 1997]. The mechanisms by which galectin-3 modulates the interactions of cells with extracellular matrices is not well defined, and may vary in different cell types and at different stages of differentiation or transformation. For example, it has been demonstrated that galectin-3 expression is crucial for transformed cells to acquire the anchorage independent growth in soft agar [Raz et al., 1990; Makker et al., 1995]. Recent studies suggest that galectins modulate cell to extracellular matrix interactions in a novel fashion by interaction with integrins such as $\alpha 7\beta 1$ or $\alpha 1b1$ [Gu et al., 1994; ochieng et al., 1998].

It is presumed that cells interact with elastin via the non-integrin 67 kDa elastin/laminin receptor [Lesot et al., 1983; Malinoff and Wicha, 1983; Rao et al., 1983]. Whereas the mature receptor on the cell surface is 67 kDa, its full-length gene encodes only a 37 kDa precursor protein [Yow et al., 1988; Rao et al., 1989]. It is believed the precursor is bonded to a ~30 kDa protein to form the mature chimeric receptor. Since the discovery of this receptor, it has been known that it has galectin-like properties because lactose modifies its biological activities. More recently, the work of Buto et al. [1998], suggested that the 67 kDa receptor is a heterodimer stabilized by strong intramolecular hydrophobic interactions, carried by fatty acids bound to the 37 kDa precursor and to a galectin-3 cross-reacting molecule. We have therefore hypothesized that galectin-3 is part of the 67 kDa elastin/laminin receptor complex

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*Correspondence to: Dr. Josiah Ochieng, Meharry Medical College, 1005 D.B. Blvd., Nashville, TN 37208.
E-mail: ochien10@ccvax.mmc.edu

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and contributes to the cell-elastin or cell-laminin interactions.

On the surface of mesenchymal cells, there are high affinity receptors for elastin-peptides. These peptides are capable of triggering intracellular signaling which may be responsible for synthesis or recruitment of cell surface ~120 kDa receptors for insoluble elastin [Groult et al., 1991]. It is possible that similar signaling responses may be triggered in non-mesenchymal cells. Breast carcinoma cells interact well with insoluble elastin [Parsons et al., 1991], and the elastin receptors in these cells may be activated in a fashion similar to the mesenchymal cells. Despite recent progress in the characterization of the 67 kDa elastin receptor, our knowledge of cell-elastin interactions still lag behind the well characterized cell-laminin or cell-collagen interactions. It is likely that in regards to tumor growth either in situ or in micrometastases, cell-elastin interactions are as important as the interactions of cells with either laminin or collagen IV.

We hereby demonstrate that galectin-3 at high extracellular concentrations, can ligate breast carcinoma cells to elastin. We further demonstrate that galectin-3 is tightly associated with insoluble elastin, an association which can be downregulated by lactose. Our data also suggest that galectin-3 is associated with soluble tropoelastin intracellularly and is an integral part of the cell to elastin receptor complex.

## MATERIALS AND METHODS

Human breast carcinoma cell lines BT-549; Sk-Br-3; MDA-MB-435; and 11–9-1–4 (derived from BT-549) [Makker et al., 1995] were obtained from Dr. Avraham Raz, Karmanos Cancer Institute. All the cell lines were cultured in DMEM (Sigma) supplemented with 100 µg/ml penicillin-streptomycin, 2.5 µg/ml Fungizone, 20 ng/ml epidermal growth factor, 98 ng/ml cholera toxin, 10% heat inactivated fetal bovine serum, 2 mM glutamine, and non-essential amino acids. The cultures were maintained at 37°C in a humidified atmosphere of 5% $CO_2$ and 95% air. Recombinant galectin-3 was isolated and purified as described [Ochieng et al., 1993].

### Ligation of Breast Carcinoma Cells to Elastin by Recombinant Galectin-3

Insoluble elastin was washed extensively with PBS containing 1 M NaCl to dissociate any non-specifically bound protein. The elastin fibers were then resuspended in PBS at 4 mg/ml and the suspension (100 µl/well) added to the wells of an ELISA micro-titer plate (Immulon 1B, Dynex Technologies) and incubated overnight at 37°C. The wells were then washed once with PBS and 200 µl of 3% heat inactivated fatty acid free bovine serum albumin in PBS added to each well to block non-specific sites for 1 h at 37°C. The wells were once more washed with PBS and serumless, calcium-free DMEM/F12 medium containing increasing doses (0–25 µg/well) of galectin-3 added to each well and allowed to incubate for 15 min at 37°C. The breast carcinoma cells, BT-549 (subclone 11–9-1–4) cells were then added to the wells at $5 \times 10^4$ cells/well in the serumless medium and allowed to incubate for 1 h at 37°C. The same number of cells/well were also plated in wells coated with 3% bovine serum albumin (open bars) in the presence of galectin-3 (0–25 µg/well) and incubated as above. The wells were then washed (3×) with serumless medium and the number of cells ligated to elastin per well determined by the Alamar blue method as previously described [Warfield et al., 1997].

To test whether the cells adhere to glycoproteins which may be associated with elastin fibers such as fibrillin, the elastin (5 mg/ml) was treated with anhydrous hydrazine and 1% hydrazine sulfate overnight at 80°C. The solubilized elastin was then used to coat the wells of a microtiter plate and cellular adhesion performed as described above.

### Growth of Breast Carcinoma Cells on Elastin

Insoluble elastin was washed and added to ELISA microtiter plates as described above. Breast carcinoma cells (galectin-3 expressing and null expressing cell lines, $2 \times 10^4$ cells/well) were then added to wells containing elastin after blocking with BSA, in DMEM/F12 medium containing 10% serum and allowed to grow for up to 10 days in a humidified $CO_2$ incubator. The cells were then photographed using a digital camera (Kodak) and the images analyzed by Adobe Photoshop.

### Binding of Galectin-3 to Elastin

Insoluble elastin was washed with high salt and added to ELISA microtiter plate as described above. After blocking the non-specific sites with 3% bovine serum albumin, serially diluted aliquots of recombinant galectin-3 (0–16 µg/well) were added to the wells in duplicates

in the absence and presence of 200 mM lactose. To demonstrate elastin binding specificity, galectin-3 in the same concentration range was also added to wells coated with BSA alone. After 1 h of incubation at 37°C, the wells were washed twice with PBS containing 0.05% tween and 100 µl of rabbit polyclonal antibodies to galectin-3 (1:500) added to each well and incubated at 37°C for 30 min. The wells were then rinsed 3× with PBS and 50 µl of biotinylated goat anti-rabbit IgG (Vectastain-ABC kit) added to each well and incubated for 5 min at 37°C. After washing the wells (3×) with PBS, 50 µl of Vectastain ABC reagent was added to each well and incubated for a further 5 min at 37°C. The wells were then washed extensively (6×) with PBS and then alkaline phosphate substrate (Blue PhosTM) added and absorbance (650 nm) determined by a microplate reader (Dynex Tech.).

### Immunoprecipitation of Elastin-Galectin-3 Complex

In order to establish the physiological relevance of elastin-galectin-3 interactions, we questioned whether the two proteins are associated either intracellularly or on the cell surface of breast carcinoma cells which express both galectin-3 and elastin. The cells were lysed in lysis buffer (calcium/magnesium free PBS containing, 0.5% NP 40, 1 mM EDTA, 2 mM PMSF, pH 7.5). The lysate was pre-cleared by incubating for 2 h with protein A/G agarose and aliquots (200 µg of protein each) of the lysate incubated with 0, 5, 10, and 20 µg of recombinant galectin-3 for 2 h at 4°C followed by either rabbit pre-immune serum or rabbit polyclonal anti-galectin-3 antibodies (10 µg/tube) for 10 h at 4°C in eppendorf tubes. Protein A/G agarose was then added to each tube and allowed to incubate for 2 h at 4°C. The agarose was then washed 5× with PBS containing 0.05 % tween and boiled for 5 min with 1X SDS-sample buffer. The samples were then analyzed by 10% SDS-PAGE, transferred to immobulin-P membrane and probed with mouse anti-human elastin which recognizes bands of tropo-elastin in Western blots. The membranes were washed and probed with peroxidase labeled sheep anti-mouse IgG, followed by incubation with Amhersham chemiluminescence reagents and exposed to X-ray film. In another set of experiments, the lysates (200 µg of protein each) were incubated with either non-immune mouse antibodies or mouse monoclonal anti-elastin (Sigma) after pre-clearance. The immunoprecipitation was done as described above, and the membranes probed with rat monoclonal anti-galectin-3 (TIB 166) [Warfield et al., 1997]. The membranes were washed and then probed with peroxidase labeled goat anti-rat IgG and the bands visualized as described above.

## RESULTS

### Interactions of Breast Carcinoma Cells With Elastin

Strong adhesion of cells to extracellular matrix proteins depend on a number of factors, such as the activation state of the cell surface receptors and optimal biochemical conditions such as pH, divalent cations, and incubation temperatures. In the case of cell to elastin adhesion, despite the lack of involvement of integrins, divalent cations, and serum factors are needed for optimal interaction with insoluble elastin [Ochieng et al., unpublished data]. The divalent ions and serum factors may be necessary for the activation or recruitment of the 67 kDa elastin receptor. In analyzing the involvement of galectin-3 in cell to elastin interaction, we employed conditions which were unfavorable for integrins (lack of divalent ions). Biological activity of galectin-3 is independent of divalent cations and serum, especially when using exogenously supplied protein. Serum was excluded in the medium because serum proteins such as fibronectin and fetuin could potentially interact with elastin and promote cellular adhesion via other receptors.

In the adhesion assays, the insoluble elastin after washing in buffer containing high salt, was immobilized very well to the floor of the wells and could not be removed by gentle washing. We have consistently shown that galectin-3 expressing breast carcinoma cells such as 11–9-1–4 and MDA-MB-435 interact much better with elastin compared to low galectin-3 expressing cells such as SK-Br-3. In our hands, we have repeatedly observed that approximately 10–20% of the galectin-3 expressing cells when added to micro-titer wells coated with elastin will adhere within 1 h of incubation at 37°C. In the case of low galectin-3 expressing cells, less than 5% of the added cells adhere after 1 h of incubation (data not shown). This phenomenon is true for other extracellular matrix proteins, laminin, and collagen IV [Warfield et al. 1997].

We therefore wanted to determine whether exogenously added galectin-3 could improve the interaction of breast carcinoma cells with elastin. Our data (Fig. 1) demonstrate that galectin-3 by itself can significantly promote the adhesion of cells to immobilized elastin. The galectin-3 mediated ligation of cells to elastin was concentration dependent. It is likely that for cells to interact optimally with elastin, secreted galectin-3 is concentrated on the cell surface to ligate or improve their adhesion to elastin. If this is so, then galectin-3 mediated adhesion of cells to elastin could be a physiologically relevant mechanism of cell-elastin interaction. The experiment was repeated three times with BT-549 clone 11–9-1–4, and once with MDA-MB-435. Both are tumorigenic cells lines of breast cancer. In all cases, high concentrations of galectin-3 were capable of ligating cells to elastin. We estimated that approximately 40–50% of the cells added to the wells were ligated to elastin at 25 μg/ml of galectin-3. Similar concentrations of galectin-3 were unable to ligate the cells to wells coated with BSA alone (Fig. 1).

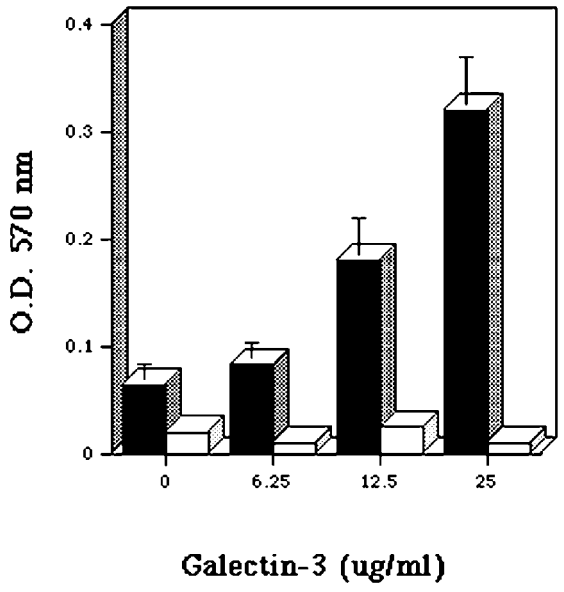


**Fig. 1.** The ligation of breast carcinoma, BT-549, subclone 11–9-1–4 cells to elastin by galectin-3. The cells in calcium free, serumless DMEM/F12 medium were plated at $5 \times 10^4$ cells/well in elastin coated microtiter wells (solid bars) in the presence of recombinant galectin-3 (0–25 μg/well). The same number of cells/well were also plated in wells coated with bovine serum albumin (open bars) in the presence of galectin-3 (0–25 μg/well). The adherent cells were determined after 1 h. The experiment was repeated three times with 11–9-1–4 cells.

To further explore the interaction of breast carcinoma cells with elastin, the cells were added to elastin coated wells and allowed to incubate for up to 10 days. In this experiment, we were interested in testing the hypothesis that galectin-3 expressing cells have a higher propensity to adhere and proliferate on elastin compared to low galectin-3 expressing cells. By day 3 of incubation of the various cell lines with elastin, we consistently observed that the cells (11–9-1–4) which express high levels of galectin-3 [Makker et al., 1995; Warfield et al., 1997], interacted very well with insoluble elastin (Fig. 2A). There were numerous cells (arrow heads) associated with individual elastin fibers (arrows). This was in contrast to the cells (SK-Br-3) with little or no expression of galectin-3 (Fig. 2B). In this case, there were fewer cells associated with elastin fibers and were easily detached by washing. Interestingly, the cells which had better interactions with elastin (high galectin-3 expression) also had a tendency to proliferate while on the elastin fibers or in close proximity to the fibers as shown in Figure 2A. After 7 days of growth on elastin fibers, the galectin-3 expressing cells (11–9-1–4) literally covered the elastin fibers, resulting in expanding colonies of proliferating cells (Fig. 2C). The galectin-3 null expressing cells (SK-Br-3), on the other hand, showed little or no proliferation on elastin after 7 days of growth (Fig. 2D). The experiment was repeated four times with similar results each time. The experiment was also repeated with MDA-MB-435 (high galectin-3 expression) and BT-549 (lack galectin-3 expression) cell lines. The MDA-MB-435 cells as expected proliferated rapidly on elastin fibers, while BT-549 only interacted marginally with elastin (data not shown).

### Interaction of Galectin-3 With Elastin

To explain the ability of galectin-3 to ligate cells to elastin, we questioned whether the lectin interacts specifically with insoluble elastin. Indeed in five separate experiments, we demonstrated by ELISA that galectin-3 interacts very strongly with insoluble elastin. The binding curve was saturable and lactose dependent (Fig. 3). Similar concentration of galectin-3 did not bind to bovine serum albumin coated wells (nonspecific binding). To eliminate the possibility that galectin-3 interacts via the sugar moieties which may be present in elastin, the elastin

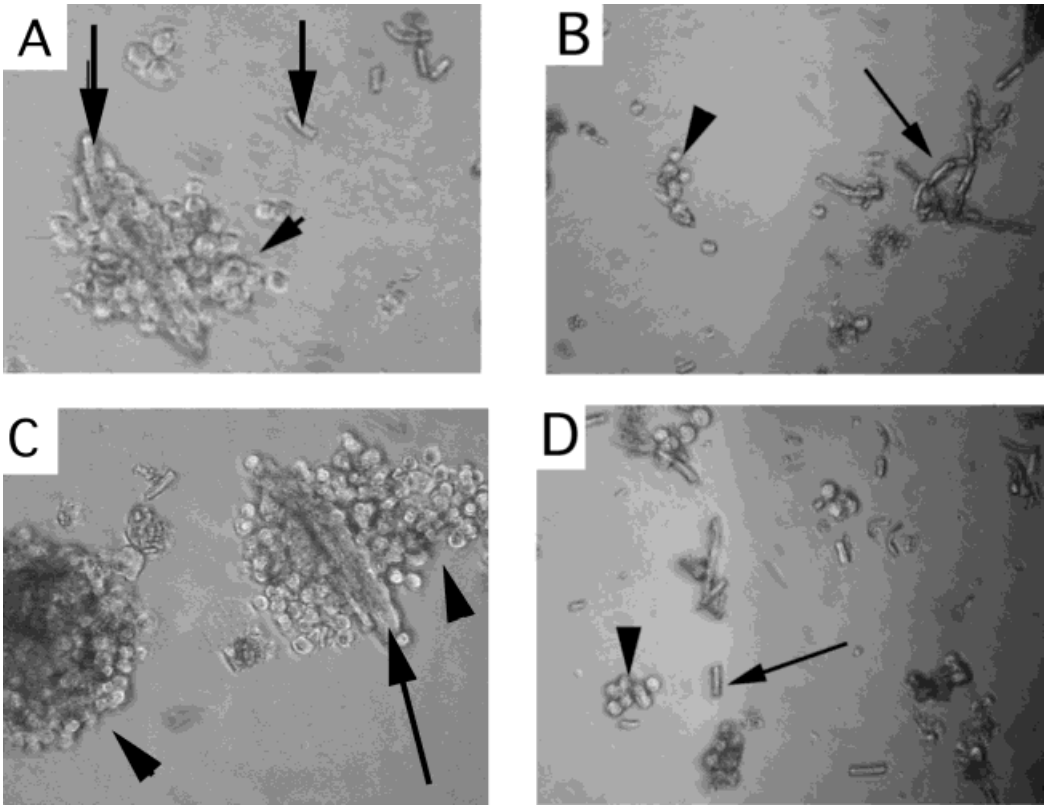


**Fig. 2.** Growth of galectin-3 expressing and null expressing cell lines on elastin. The wells of a microtiter plate were coated with elastin as described in Materials and Methods. The cells ($2 \times 10^4$ cells/well) were then added to the elastin coated wells in DMEM/F12 medium containing 10% bovine serum and allowed to grow for 3 days (**A,B**) or 7 days (**C,D**). Galectin-3 expressing 11–9-1–4 cells (**A,C**) and SK-Br-3 (**B,D**). The cells are depicted by arrow-heads and elastin-fibers by arrows.

fibers were treated with anhydrous hydrazine which cleaves glycosidic bonds. The anhydrous hydrazine completely solubilized the elastin after about 5 h of the treatment. The addition of galectin-3 to wells coated with hydrazine solubilized elastin yielded saturable binding curves similar to Figure 3 (data not shown), suggesting that galectin-3 was directly interacting with peptide domains of elastin in a novel fashion.

To further explore the interaction of galectin-3 with elastin, we questioned whether intracellularly expressed elastin (tropoelastin) is associated with galectin-3 in cells which express both proteins. It has been demonstrated that whereas tropoelastin is mainly synthesized by fibroblasts in the mammary gland, breast epithelial cells can also express the protein [Krishnan and Cleary, 1990]. Our data clearly demonstrate that polyclonal antibodies to galectin-3 can bring down a complex of proteins containing tropoelastin (with bands in the range of ~55–70 kDa) from lysed breast carcinoma cells (Fig. 4A). Non-immune rabbit serum (control) failed to specifically immunoprecipitate the complex (Fig. 4A, lane 1). Addition of excess recombinant galectin-3 to the lysates (lanes 3 to 5) did not increase the amount of immunoprecipitable complex, implying that the complex probably exists intracellularly in a saturated state with all the galectin-3 binding sites on tropoelastin occupied. The complex was also brought down with mouse monoclonal antibodies against elastin. When the membrane was probed with rat anti-galectin-3, a strong band at 30 kDa (galectin-3) and a smaller band at ~62 kDa, were observed (Fig. 4B). The data strongly suggest that the association between galectin-3 and elastin is a physiologically relevant phenomenon. Studies are currently ongoing to evaluate further the nature of this complex, including the ~62 kDa protein which cross-reacts with anti-galectin-3 antibodies.

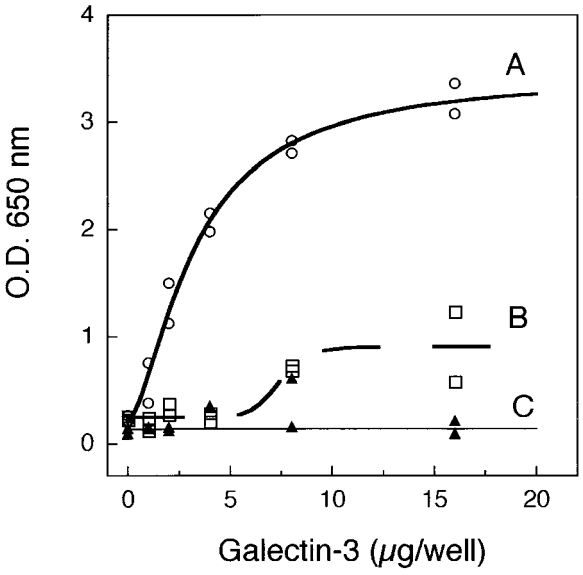


**Fig. 3.** Binding of galectin-3 to elastin. The wells of a microtiter ELISA plate were coated with elastin as described in Materials and Methods. Recombinant galectin-3 (0–16 μg/well) was then added to the wells in duplicates in the absence of lactose (circles; line **A**) or presence of 200 mM of lactose (squares; line **B**). Galectin-3 in the same concentration range was also added in duplicates to wells coated with bovine serum albumin alone (triangles; line **C**). After 1 h of incubation at 37°C, galectin-3 bound to elastin was determined by ELISA as described in Materials and Methods. The absorbance of the alkaline phosphate substrate was determined at 650 nm.

## DISCUSSION

In the present study, we have demonstrated that galectin-3 associates in a novel fashion with both the soluble and insoluble elastin. This specific association could be important in the regulation of cell-elastin interactions. The adhesive interactions of cells with elastin is not well defined compared to the other extracellular matrix proteins, because the main physiological function of elastin is to impart elasticity to vertebrate elastic tissues. Nevertheless, it has been demonstrated that insoluble elastin as well as elastin peptides are capable of promoting not only cellular adhesion, but also proliferation [Parsons et al., 1991; Jung et al., 1998]. It is probable that in the case of certain primary as well as metastatic tumors growing in elastin rich tissues such as the lungs, their interaction with elastin is pivotal to their proliferative potential and formation of micrometastases in those tissues [Timar et al., 1991; Svitkina and Parsons, 1993]. For example, in the case of breast elastosis, interaction of the tumor cells with excess elastin in the breast may exacerbate tumor growth [Kao et al., 1986; Khatun et al., 1992].

It is established that the 67 kDa elastin/laminin receptor has galectin-like properties because lactose and anti-galectin-1 antibodies are capable of modifying its biological activities [Mecham et al., 1989]. This, taken together with the recent studies suggesting galectin-3 may be a novel component of the 120 kDa elastin/laminin receptor complex [Buto et al., 1998], prompted us to question whether galectin-3 has a direct role in cell-elastin interactions. Presently it is not clear which part of the chimeric 67 kDa receptor protein is responsible for strong cellular adhesion to elastin. Sequences in the 37 kDa precursor protein have been shown to interact with elastin peptides [Castronovo et al., 1991]. However the contribution of the ~30 kDa component in elastin binding is virtually unknown.

The ability of galectin-3 to interact with elastin in a lactose dependent manner suggests that this is a novel interaction. The interaction may involve both the R- and carbohydrate recognition domains which have been shown to participate in non-covalent homodimeriation of the molecule leading to positive cooperativity [Hsu et al., 1992; ochieng et al., 1993; Kuklinski and Probsteimer, 1998]. To explain the ability of galectin-3 to ligate the cells to elastin, we postulate that the exogenously supplied recombinant galectin-3 forms a covalent complex with the 37 kDa precursor of the 67 kDa elastin/laminin receptor on the cell surface resulting in the mature protein which in turn promotes the cellular adhesion to elastin. Alternatively high concentrations of galectin-3 may form higher order oligomers by positive cooperativity [Hsu et al., 1992; ochieng et al., 1993], with some molecules binding specifically to elastin and others to its cell surface expressed ligands such as lysosomal associated membrane proteins [Do et al., 1990], thereby acting as a bridge which links the cells to elastin coated wells (Fig. 5). Other cellular mechanisms may also be involved. For example, cell-elastin interactions may take place in two or more phases. Galectin-3 on the cell surface, may form a temporary bridge between cells and insoluble elastin, followed by the full participation of the 67 kDa in the adhesion as a late response.

We compared growth potentials of various cell lines on elastin, to further implicate galectin-3 in cell-elastin interactions. All the galec-

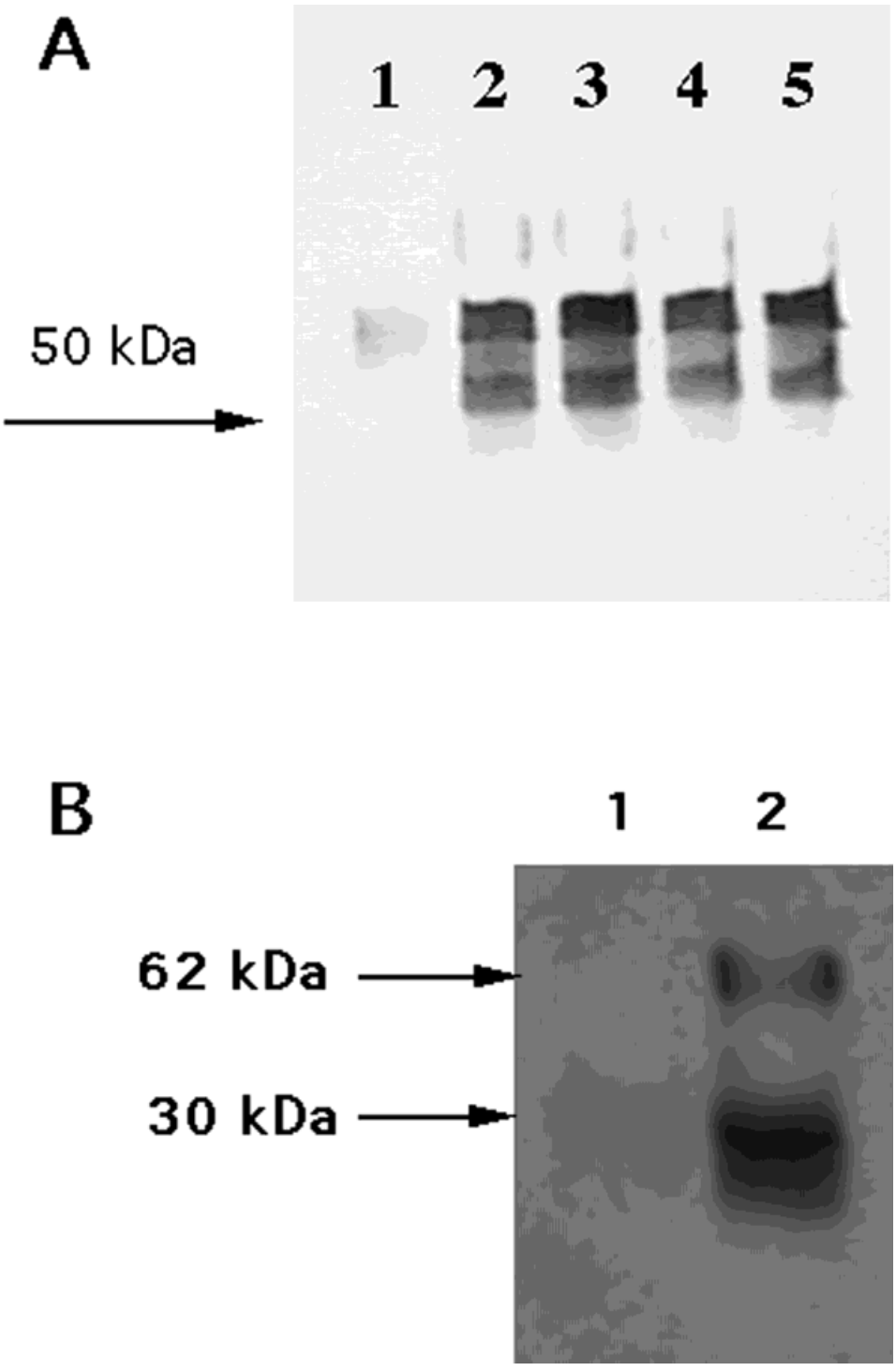


**Fig. 4.** Association of Elastin and galectin-3. Galectin-3 expressing breast carcinoma cells were lysed and the lysate immunoprecipitated with either rabbit pre-immune serum (**A, lane 1**) or rabbit polyclonal antibodies to recombinant human galectin-3 (**A, lanes 2–5**). In lanes 2–5, the lysates were incubated with 0, 5, 10, and 20 μg of recombinant galectin-3 for 2 h at 4°C prior to the addition of galectin-3 antibodies. The samples then resolved by 10% reducing SDS-PAGE, blotted, and the membrane probed with mouse monoclonal antibodies to elastin. The bands represent tropoelastin ~62–67 kDa. The immunoprecipitation was also done with either non-immune mouse serum (**B, lane 1**) or mouse monoclonal anti-elastin (**B, lane 2**). In this case the membrane was probed with rat monoclonal anti-galectin-3. The galectin-3 band (30 kDa) as well as a band which most likely represents a galectin-3 dimer (~62 kDa) are represented in **B, lane 2**.

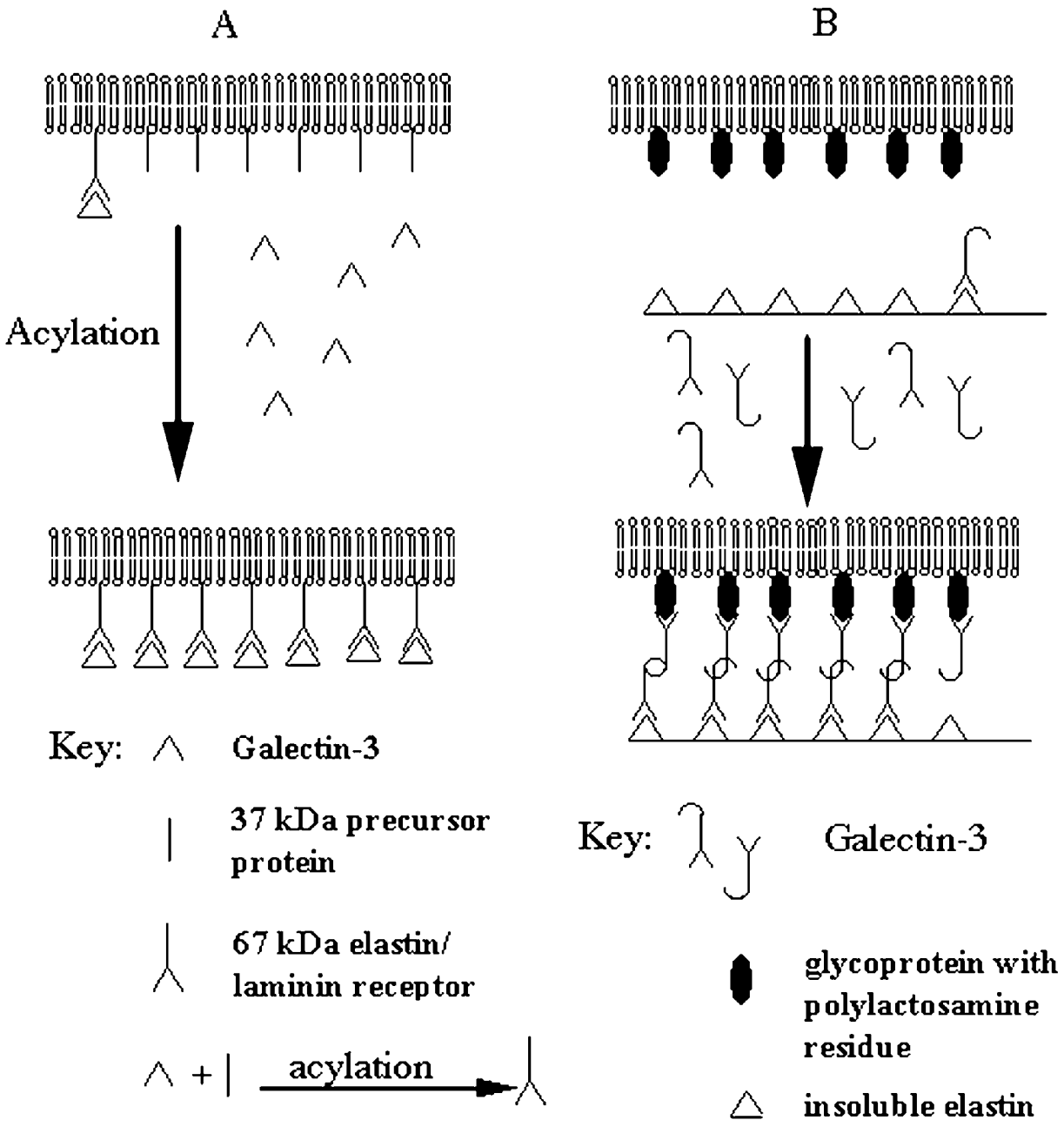


**Fig. 5.** A model depicting two possible ways by which galectin-3 ligates cells to elastin. In **A**, galectin-3 and the precursor of 67 kDa laminin receptor are joined by acylation to form the mature 67 kDa laminin receptor which is then used for adhesion to elastin. In **B**, some of the galectin-3 molecules interact with elastin while others with polylactosamine containing glycans on the cell surface via their carbohydrate recognition domains. The galectin-3 molecules then interact with each other via their R-domains, forming bridges which ligate the cells to the elastin.

tin-3 expressing cell lines proliferated rapidly on elastin while the galectin-3 null expressing cell lines only interacted marginally with elastin. Presently we do not know whether galectin-3 expression is the rate limiting step in such interactions. One approach to address this quandary is to stably transfect the galectin-3 expressing cell lines with anti-sense galectin-3 gene and show whether the transfected cells have reduced proliferative capacity on elastin. Galectin-3 expression has already been demonstrated to play a significant modulatory role in the interaction between cells and two extracellular matrix proteins, laminin and collagen IV [Warf-

ield et al., 1997]. Interestingly, the 67 kDa elastin/laminin receptor can also mediate the interaction of cells with collagen [Minafra et al., 1992].

The ability of anti-galectin-3 polyclonal antibodies to immunoprecipitate a complex consisting of tropoelastin, suggests that galectin-3 is tightly associated with the intracellular soluble elastin. Presently, we do not know the significance of this association. It could be a novel pathway by which galectin-3 is secreted to the extracellular space since this protein lacks the signal peptide [Barondes et al., 1994]. We cannot however, rule out the possibility that the complex also comprises the 67 kDa receptor which has been shown to be associated with tropoelastin [Hinek and Rabinovitch, 1994]. Therefore the association of galectin-3 and intracellularly expressed tropoelastin and possibly the insoluble extracellular elastin implies a modulatory role in cell to elastin interactions. Moreover this modulatory role of galectin-3 may extend to the interaction of cells with other extracellular matrix proteins such as laminin [ochieng and Warfield, 1995].

In summary, we have demonstrated that galectin-3 on the cell surface has the propensity to ligate or increase the adhesion of breast carcinoma cells to insoluble elastin. We have also demonstrated that galectin-3 interacts specifically with both soluble and insoluble elastin. It appears that galectin-3 uses its carbohydrate recognition domain in its interaction with elastin. The enhanced interaction of breast carcinoma cells (which express galectin-3) with elastin, further implicates galectin-3 in cell to elastin interactions. We also postulate based on our data, that galectin-3 may cooperate with the 67 kDa elastin/laminin receptor protein or its precursor to regulate cell-elastin interactions. Furthermore, it is tempting to speculate that the expression of galectin-3 and the 67 kDa elastin-laminin receptor confer on breast carcinomas, the propensity to form micrometastasis on elastin-rich tissues such as the lungs.

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