Galectins-3 and -7, but not Galectin-1, Play a Role in Re-epithelialization of Wounds*

Disorders of wound healing characterized by impaired or delayed re-epithelialization are a serious medical problem. These conditions affect many tissues, are painful, and are difficult to treat. In this study, using cornea as a model, we demonstrate for the first time the importance of carbohydrate-binding proteins galectins-3 and -7 in re-epithelialization of wounds. In two different models of corneal wound healing, re-epithelialization of wounds was significantly slower in galectin-3-deficient (gal3−/−) mice compared with wild-type (gal3+/+) mice. In contrast, there was no difference in corneal epithelial wound closure rates between galectin-1-deficient and wild-type mice. Quantitation of the bromodeoxyuridine-labeled cells in gal3−/− and gal3+/+ corneas revealed that corneal epithelial cell proliferation rate is not perturbed in gal3−/− corneas. Exogenous galectin-3 accelerated re-epithelialization of wounds in gal3+/+ mice but, surprisingly, not in the gal3−/− mice. Gene expression analysis using cDNA microarrays revealed that healing corneas of gal3−/− mice contain markedly reduced levels of galectin-7 compared with those of gal3+/+ mice. More importantly, unlike galectin-3, galectin-7 accelerated re-epithelialization of wounds in both gal3−/− and gal3+/+ mice. In corresponding experiments, recombinant galectin-1 did not stimulate the corneal epithelial wound closure rate. The extent of acceleration of re-epithelialization of wounds with both galectin-3 and galectin-7 was greater than that observed in most of the published studies using growth factors. These findings have broad implications for developing novel therapeutic strategies for treating nonhealing wounds.

In a number of organ systems including cornea, skin, and gastrointestinal tract, disorders of wound healing characterized by impaired or delayed re-epithelialization and associated persistent epithelial defects constitute a serious medical problem (1–4). Persistent epithelial defects of the cornea may progress through the anterior stroma, resulting in stromal ulceration and, in the worst cases, perforation of the tissue with significant visual loss (3, 4). Delayed re-epithelialization and persistent epithelial defects are also characteristic of chronic wounds in the elderly, decubitus ulcers, and venous stasis ulcer of the skin, conditions that together affect millions of individuals worldwide (1, 2). In most cases, failure of re-epithelialization is not attributed to inadequate cell proliferation but the result of a reduced potential of the epithelium to migrate across the wound bed (5–7). Cell migration is a complex biological process that entails sequential adhesion and release from the substrate, a process in which cell-matrix interactions play a key role (8, 9). Whereas the regulation of cell-matrix interactions is a poorly understood process, it is known that in many instances, cell attachment to the matrix is mediated by recognition between extracellular matrix (ECM) molecules and transmembrane integrin receptors. Recent studies have provided evidence that members of the galectin class of β-galactoside-binding proteins (10–13), in particular galectin-1 and galectin-3, also have the potential to mediate cell-matrix interactions by a novel mechanism (14–17). Both lectins are expressed in inflammatory cells and in epithelia and fibroblasts of various tissues (10–13). They are found on the cell surface within ECM and in the cytoplasm of cells and are thought to influence cell-matrix adhesion by binding to the ECM and cell surface-glycosylated counter receptors (e.g. certain isoforms of laminin, fibronectin, vitronectin, and integrins). In addition, galectin-3 is found in the nucleus of the cells and may influence cell-matrix interactions indirectly by influencing the expression of well known cell adhesion molecules (e.g. αvβ3 and αvβ5 integrins) (16, 17) and cytokines (e.g. IL-1) (18). Although all members of the galectin family bind to β-galactoside residues, each galectin has unique specificities for more complex oligosaccharides; therefore, different members of the galectin family may bind distinct glycoconjugate receptors, resulting in specific downstream effects. Here we demonstrate that galectin-3 but not galectin-1 plays a role in re-epithelialization of corneal wounds and that another member of the galectin family, galectin-7, is also involved in the wound healing process.

EXPERIMENTAL PROCEDURES

Wound Healing Experiments—All animal treatments in this study conformed to the Association for Research in Vision and Ophthalmology Resolution on the Use of Animals in Vision Research and the recommendations of the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Gal3−/− mice were generated by targeted interruption of the galectin-3 gene as described previously (19). Gal3−/− mice were provided evidence that members of the galectin class of β-galactoside-binding proteins (10–13), in particular galectin-1 and galectin-3, also have the potential to mediate cell-matrix interactions by a novel mechanism (14–17). Both lectins are expressed in inflammatory cells and in epithelia and fibroblasts of various tissues (10–13). They are found on the cell surface within ECM and in the cytoplasm of cells and are thought to influence cell-matrix adhesion by binding to the ECM and cell surface-glycosylated counter receptors (e.g. certain isoforms of laminin, fibronectin, vitronectin, and integrins). In addition, galectin-3 is found in the nucleus of the cells and may influence cell-matrix interactions indirectly by influencing the expression of well known cell adhesion molecules (e.g. αvβ3 and αvβ5 integrins) (16, 17) and cytokines (e.g. IL-1) (18). Although all members of the galectin family bind to β-galactoside residues, each galectin has unique specificities for more complex oligosaccharides; therefore, different members of the galectin family may bind distinct glycoconjugate receptors, resulting in specific downstream effects. Here we demonstrate that galectin-3 but not galectin-1 plays a role in re-epithelialization of corneal wounds and that another member of the galectin family, galectin-7, is also involved in the wound healing process.

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The abbreviations used are: ECM, extracellular matrix; mAb, monoclonal antibody; BrdUrd, bromodeoxyuridine; RT, reverse transcription; MEF, mouse embryonic fibroblasts.

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and gal3+/− mice were obtained by interbreeding gal3+/− mice and carried as separate lineages. Galectin-1-deficient mice originally prepared by Poirier and Robertson (20) were made available by Drs. Douglas N. Cooper, (University of California, San Francisco, CA) and Carrie Miceli (University of California, Los Angeles, CA). Both gal1+/− and gal3+/− mice are fertile and viable and do not exhibit any overt defects.

To produce corneal wounds, mice were anesthetized by an intramuscular injection of 1.25% avertin (0.2 ml/g body weight) (Aldrich). Preparative eye drops (Alcain, Alcon Labs, Inc., Fort Worth, TX) were applied to the cornea as a topical anesthetic. We produced 2-mm corneal wounds on the right eye of each animal by: (i) transepithelial excimer laser ablations (2-mm optical zone; 42–44-micron ablation depth, phototherapeutic keratectomy mode) using Summit Apex Plus Excimer Laser (Summit, MA); (ii) placing alkali (0.5 M NaOH) soaked filter discs on the surface of the cornea for 2 min; or (iii) abrasion using Algerbrush® (Lago Vista, TX). The left eye served as a control. Following surgery, all of the animals received buprenorphine (intramuscular, 0.2 ml of 0.3 mg/ml Buprenex, Reckitt and Colman Pharmaceuticals, Inc., Richmond, VA) as a pain killer. Antibiotic ointment (Vetropolycin, Pharmaderm, Melville, NY) was applied, and the corneas were allowed to partially heal in vivo for 16–18 h. For healing in vitro, the eyes were excised out following surgery and were pinned down on paraplast wax in 24-well plates using 1 cm-long tips of 20-gauge needles (one eye/well).

Experiments to Test the Therapeutic Potential of Galectins for Acceleration of Re-epithelialization of Corneal Wounds—Recombinant full-length human galectin-3 and galectin-7 were produced in Escherichia coli and purified as described previously (23, 25). Recombinant full-length galectin-1 was provided by Dr. D. N. Cooper (26). Alkali-burn wounds (2-mm-diameter) were produced on both eyes of anesthetized animals of the left eyes served as controls and were incubated in the media alone. Right eyes were incubated in media containing various test reagents including: (i) gal1+/−, 3-, or 7 (5–20 μg/ml), (ii) a galactin plus 0.1 M β-lactose, or (iii) a galactin plus 0.1 M sucrose. At the end of the healing period, remaining wound areas were stained and quantitated. Each group contained a minimum of four eyes. All experiments were performed at least twice.

**Gene Expression Analysis Using cDNA Microarrays**—Transepithelial excimer laser ablations (2-mm-diameter) were produced on the right eye of 30 gal3+/− and 30 gal3−/− mice. Corneas were allowed to partially heal in vivo for 16–18 h. At the end of the healing period, animals were sacrificed, and the corneas were excised and processed for gene expression analyses using SMART cDNA technology (Clontech Laboratories, Inc., Palo Alto, CA). Total RNA was isolated using the reagents provided in the Atlas Pure Total RNA-labeling system kit (yield: 3.5 and 2.6 μg for gal3+/+ and gal3−/− corneas, respectively; A260/A280 1.48 and 1.37 for gal3+/+ and gal3−/− corneas, respectively; 28 S/18 S, 1.8 for both preparations) and was used for cDNA probe synthesis as described in the protocol for SMART cDNA synthesis and T7 Probe Synthesis (Clontech). The amplified cDNAs (500 ng) were radiolabeled using Klenow enzyme and [β-32P]ATP and then hybridized to cDNA microarrays (mouse 1.2–1 broad spectrum, ~1200 genes, Clontech). Following hybridization, the membranes were exposed to a phosphorimaging screen. Results were analyzed by Atlas Image 2.0 software (Clontech). The genes were verified by semiquantitative RTPCR, Western blot analysis, and immunohistochemical localization studies. Semiquantitative RT-PCR was performed using total RNA preparations from the corneas and gene-specific custom primers purchased from Clontech and other reagents from the Advantage 2 PCR kit (Clontech).
cell-matrix interactions. In healing corneas, the leading edge of migrating epithelium stained more intensely with mAb M3/38 compared with that in the gal3−/− mice (Fig. 1Bii) and all of the seven corneas with abrasion wounds (data not shown) (staining pattern indistinguishable from Fig. 1Bii). Also, in healing epithelium, immunostaining was more intense at sites of cell-matrix attachment. Whereas stromal cells of normal corneas did not react with anti-galectin-3 mAb, cells in the anterior stroma under healing corneas expressed galectin-3, especially in the region under migrating epithelium (Fig. 1Bii, arrowhead). Corneas allowed to heal in organ culture showed similar results with respect to galectin-3 immunoreactivity in corneal epithelium (n = 2, excimer laser wounds) (data not shown). However, anterior stroma of corneas, which were allowed to heal in vitro, lacked cells expressing galectin-3, suggesting that galectin-3-positive cells seen in the stroma of corneas allowed to heal in vivo are most probably lymphocytes and not keratocytes. As expected, no galectin-3 immunoreactivity was detected in normal (Fig. 1Biii) and healing (Fig. 1Biv) corneas of gal3−/− mice. Also, no galectin-1 immunoreactivity was detected in the epithelia of normal (Fig. 1Bv) and healing (Fig. 1Bvi) corneas of the wild-type mice.

Re-epithelialization of Corneal Wounds Is Perturbed in gal3−/− Mice—To determine whether re-epithelialization of corneal wounds is impaired in galectin-3-deficient mice, we used two different models of corneal wound healing. Corneas with excimer laser ablations or alkali-burn wounds were allowed to partially heal in vivo for 16–18 h. 2 h before the mice were sacrificed, BrdUrd was injected. At the end of the healing period, histology sections of the corneas were stained with an anti-BrdUrd mAb, A, normal and healing corneas of gal3−/− mice stained with anti-BrdUrd. In normal, uninjured corneas, BrdUrd-labeled cells were randomly distributed throughout the epithelium. In contrast, in healing corneas, the BrdUrd-labeled cells were concentrated in the periphery. C, central cornea; P, peripheral cornea; W, wound area toward the center of the cornea; MF, migratory front, the area behind the leading edge of migrating corneal epithelium. Arrowheads indicate epithelium; arrows indicate BrdUrd-labeled cells. A similar staining pattern was seen in gal3−/− corneas (data not shown) (photographs identical to those shown for gal3−/− corneas). B, quantitation of BrdUrd-labeled cells in normal and healing corneas of gal3−/− and gal3−/− mice. For healing corneas, the number of labeled cells detected in the periphery and in the migratory front of the epithelium is shown separately. For normal corneas, values of the entire epithelium are shown together because there was no significant difference in the number of labeled cells between central and peripheral corneal epithelium. Mean ± S.E. of 15 sections derived from five healing corneas and 11 sections derived from four normal corneas each of gal3−/− and gal3−/− mice are shown.

![Fig. 3](image)

**FIG. 3.** Corneal epithelial cell proliferation rate is similar in gal3−/− and gal3−/− corneas. Corneas of gal3−/− and gal3−/− mice with 2-mm central epithelial wounds were allowed to partially heal in vivo for 16–18 h. 2 h before the mice were sacrificed, BrdUrd was injected. At the end of the healing period, histology sections of the corneas were stained with an anti-BrdUrd mAb. A, normal and healing corneas of gal3−/− mice stained with anti-BrdUrd. In normal, uninjured corneas, BrdUrd-labeled cells were randomly distributed throughout the epithelium. In contrast, in healing corneas, the BrdUrd-labeled cells were concentrated in the periphery. C, central cornea; P, peripheral cornea; W, wound area toward the center of the cornea; MF, migratory front, the area behind the leading edge of migrating corneal epithelium. Arrowheads indicate epithelium; arrows indicate BrdUrd-labeled cells. A similar staining pattern was seen in gal3−/− corneas (data not shown) (photographs identical to those shown for gal3−/− corneas). B, quantitation of BrdUrd-labeled cells in normal and healing corneas of gal3−/− and gal3−/− mice. For healing corneas, the number of labeled cells detected in the periphery and in the migratory front of the epithelium is shown separately. For normal corneas, values of the entire epithelium are shown together because there was no significant difference in the number of labeled cells between central and peripheral corneal epithelium. Mean ± S.E. of 15 sections derived from five healing corneas and 11 sections derived from four normal corneas each of gal3−/− and gal3−/− mice are shown.
Exogenous galectin-3 stimulates re-epithelialization of corneal wounds in +/+ mice but not in −/− mice. Corneas with 2-mm alkali-burn wounds were allowed to heal in organ culture in serum-free media in the presence and absence of recombinant lectins and saccharides for 20–22 h. At the end of the healing period, wound areas were quantified and compared. A, galectin-3 did not significantly accelerate wound closure rate in gal3−/− mice. B, galectin-3 stimulated corneal epithelial wound closure in a dose-dependent manner in gal3+/+ mice. C, the stimulatory effect of exogenous galectin-3 on corneal epithelial wound closure is inhibited by β-lactose, a disaccharide that contains galactose but not by sucrose, which lacks galactose. D, unlike galectin-3, galectin-1 did not accelerate corneal epithelial wound closure in gal3−/− mice. A value of 1.0 was assigned to the healing rate of control corneas incubated in media alone. The value of corneas incubated in media containing galectins or saccharides is expressed as change in the healing rate with respect to the control corneas. Means ± S.E. of two or more experiments are shown. *, p < 0.05 compared with the other three groups in panel B; **, p < 0.05 compared with gal3 (10 μg/ml) and gal3 + Suc groups in panel C. Lac, β-lactose (0.1 m); Suc, sucrose (0.1 m).

The Rate of Corneal Epithelial Cell Proliferation Is Not Perturbed in gal3−/− Mice—To determine whether delayed re-epithelialization of corneal wounds in gal3−/− mice was because of a deficiency in the rate of corneal epithelial cell proliferation, normal and healing gal3+/+ and gal3−/− corneas were labeled with BrdUrd to identify cells undergoing DNA synthesis. It is well established that in response to corneal injury, proliferation of cells distal to the wound edge is increased, whereas that at the migratory front is decreased (28, 29). Consistent with this finding, BrdUrd-labeled cells in both gal3+/+ and gal3−/− healing corneas were seen largely in the peripheral epithelium (Fig. 3A). There was no significant difference in the number BrdUrd-labeled cells between gal3+/+ and gal3−/− corneas (Fig. 3B), suggesting that the rate of corneal epithelial cell proliferation is not perturbed in gal3−/− mice.

Exogenous Addition of Galectin-3 Stimulates Corneal Epithelial Wound Closure in gal3+/+ Mice but Not in gal3−/− Mice—Having demonstrated that the corneal epithelial wound closure rate is perturbed in gal3−/− mice, it was of interest to determine whether exogenous galectin-3 would stimulate re-epithelialization of corneal wounds in organ culture. In this study, the corneas of gal3+/+ and gal3−/− mice with alkali-burn wounds were incubated in serum-free media in the presence and absence of varying amounts of recombinant galectin-3. After a 20–22-h healing period, the remaining wound areas were quantified. The exogenous galectin-3 had no influence on the rate of re-epithelialization of corneal wounds in gal3−/− mice (Fig. 4A), but it stimulated the rate of wound closure in a concentration-dependent manner in gal3+/+ mice (Fig. 4B). Overall, the extent of acceleration of re-epithelialization of wounds was 43 and 71% in the presence of 10 and 20 μg/ml galectin-3, respectively. The stimulatory effect of galectin-3 on corneal epithelial wound closure was specifically inhibited by a competing sugar, β-lactose, but not by an irrelevant disaccharide, sucrose (Fig. 4C). In corresponding experiments, recombinant galectin-1 did not stimulate the corneal epithelial wound closure rate (Fig. 4D).

Healing gal3−/− Corneas Express Reduced Levels of Galectin-7—In an attempt to understand the reason that re-epithelialization of corneal wounds is perturbed in gal3−/− mice and why gal3−/− corneas are not responsive to exogenous galectin-3, we compared gene expression patterns of healing gal3+/+ and gal3−/− corneas using cDNA microarrays. The expression of 16 genes was up-regulated, and that of 13 genes was down-regulated over 5-fold in the healing gal3+/+ corneas compared with healing gal3−/− corneas. A list of all differentially expressed genes can be viewed on our web site: www.neec.com/MicroarrayData.html. Of the 29 genes exhibiting altered expression pattern in healing gal3+/+ corneas, galectin-7, another galactose-binding protein, appeared to be the most relevant to the current study and was selected for further investigation. Gene expression analysis revealed that healing corneas of gal3−/− mice contained −12-fold less gene transcripts for galectin-7 (Fig. 5A) compared with the healing corneas of the
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Wild-type mice. That healing corneas of galectin-3−/− mice contain reduced levels of galectin-7 transcripts was further confirmed by semiquantitative RT-PCR (Fig. 5B). Western blot analysis using detergent extracts of healing galectin-3−/− and galectin-3+/− corneas (Fig. 5C) and immunohistochemical studies using paraffin sections of the corneas (Fig. 5D) revealed that healing corneas of galectin-3−/− mice contain markedly reduced levels of galectin-7 protein compared with those of the wild-type litters. Also, galectin-3−/− mouse embryonic fibroblasts (MEF) grown in cell culture expressed reduced levels of galectin-7 compared with galectin-3+/- MEF cultures (Fig. 5E). Both semiquantitative RT-PCR and Western blot analyses were performed at least twice on each sample with reproducible results.

Galectin-7 Stimulates Re-epithelialization of Wounds in galectin-3−/− Corneas—In this study, the corneas of galectin-3+/− and galectin-3−/− mice with alkali-burn wounds were incubated in serum-free media in the presence and absence of recombinant galectin-7. After a 20–22-h healing period, remaining wound areas were quantified. Unlike galectin-3 (Fig. 4A), galectin-7 accelerated the re-epithelialization of wounds in galectin-3+/− corneas (Fig. 6A). The stimulatory effect of galectin-7 on corneal epithelial wound closure was also specifically inhibited by a competing sugar, β-lactose, but not by sucrose (Fig. 6A). Galectin-7 also accelerated the re-epithelialization of wounds in galectin-3−/− corneas (Fig. 6B).

DISCUSSION

In this study, we demonstrate that galectin-3 plays a role in the re-epithelialization of corneal wounds. First, immunohistochemical studies revealed that galectin-3 is located in high density at sites of corneal epithelial cell-matrix adhesion, an ideal location for influencing cell-matrix interactions and cell migration. Second, in two different models of corneal wound healing, re-epithelialization of corneal wounds was significantly slower in the galectin-3−/− mice compared with that in wild-type mice. In contrast, there was no difference in the rate of re-epithelialization of corneal wounds between galectin-1-deficient and wild-type mice. Third, the exogenous recombinant galectin-3 stimulated re-epithelialization of corneal wounds in galectin-3−/− mice in a concentration-dependent manner. In contrast, recombinant galectin-1 had no influence. We further demonstrated that the stimulatory effect of galectin-3 on the rate of corneal epithelial wound closure can be almost completely abrogated by a competing disaccharide, β-lactose, but not by an irrelevant disaccharide, sucrose. This finding suggests that the carbohydrate recognition domain was directly involved in the beneficial effect of the exogenous lectin on the wound closure.

Regarding the mechanism by which galectin-3 may influence re-epithelialization of corneal wounds, the lectin is thought to...
mediate cell-cell and cell-matrix interactions by binding to complementary glycoconjugates containing polylactosamine chains found in many ECM and cell surface molecules, such as certain isoforms of fibronectin, laminin, and integrins (10–15). However, our findings that exogenous galectin-3 does not accelerate the re-epithelialization of wounds in gal3–/– mice suggest that intracellular galectin-3 contributes significantly to the process of wound healing, most probably, by influencing the expression of specific cell surface and/or ECM receptors, which in turn influence cell-matrix interactions and cell migration. The precedence for this notion is suggested by published studies in which galectin-3 was stably overexpressed in breast carcinoma cell lines, and it was shown that cells overexpressing the lectin expressed elevated levels of α6β1 and α5β1 integrins and exhibited enhanced adhesion to various ECM molecules including laminin, fibronectin, and vitronectin compared with parental cell lines expressing little or no galectin-3 (16, 17). In another study (30), colon cancer carcinoma cell lines transfected with galectin-3 expressed the elevated levels of a specific mucin, MUC2, a major ligand of the lectin itself (31). The fact that the stimulatory effect of exogenous galectin-3 on the rate of re-epithelialization of wounds in gal3–/– mice is lactose-

inhitable raises an intriguing possibility that intracellular galectin-3 may in fact regulate the glycosylation of the proteins, which serve as cell surface or ECM receptors of the lectin itself. That intracellular galectin-3 has the potential to act on nuclear matrix to influence complex biological processes is suggested by findings that under certain conditions the lectin can be found to be associated in the nucleus with ribonucleoprotein complexes and can act as a pre-mRNA-splicing factor (32). Also, Wang et al. (33) have demonstrated that in prostate adenocarcinoma cells, galectin-3 is associated with nuclear matrix and binds with single-stranded DNA and with RNA.

An analysis of gene expression patterns of corneas of healing gal3–/– and gal3+/– mice using mouse cDNA microarrays revealed that the healing corneas of gal3–/– mice expressed markedly reduced levels of galectin-7 compared with those of wild-type mice. Galectin-7, first reported in 1994 (12), is not as well characterized as galectins-1 and -3. To the best of our knowledge, transgenic mice deficient in galectin-7 have not been reported. Unlike galectins-1 and -3, galectin-7 exhibits a remarkable degree of tissue specificity. In adult animals, its expression is restricted to epithelia that are stratified or are destined to become stratified (34, 35). The protein is thought to be involved in cell-matrix and cell-cell interactions and in apoptosis (36–38). In general, an inverse correlation exists between galectin-7 expression and keratinocyte proliferation, and galectin-7 expression is abrogated in SV40-transformed keratinocytes as well as in cells derived from epithelial tumors. Our findings that exogenous galectin-7 does not stimulate re-epithelialization of wounds in gal3–/– corneas and that the healing gal3–/– corneas contain reduced levels of galectin-7 lead us to speculate that galectin-3 may influence the re-epithelialization of wounds, at least in part, by modulating galectin-7. Indeed, we found that unlike galectin-3, galectin-7 accelerated the re-epithelialization of wounds in gal3–/– corneas in a lactose-inhibitable manner. Also, MEF of gal3–/– mice expressed reduced levels of galectin-7. Regardless of the mechanisms involved, our findings that both galectin-3 and galectin-7 stimulate the re-epithelialization of corneal wounds have broad implications for developing novel therapeutic strategies for the treatment of nonhealing wounds. At present, the treatment of persistent epithelial defects of the cornea is a major clinical problem. Moreover, the need continues for effective treatment of chronic wounds in the elderly, decubitus ulcers, and venous stasis ulcers of the skin. A number of growth factors (epidermal growth factor, transforming growth factor-α, fibroblast growth factor, keratinocyte growth factor, and hepatocyte growth factor) known to stimulate cell proliferation have been tested for usefulness in corneal as well as cutaneous epithelial wound healing with overall disappointing results (1, 2, 39–42). The extent of acceleration of re-epithelialization of wounds was far less in most of these studies using growth factors (39, 40) than that observed with galectins in the current study. Also, the epithelium of corneas treated with growth factors such as epidermal growth factor is hyperplastic (42–44), a clearly undesirable condition. In this respect, the clinical potential of galectin-3 and galectin-7 may be more attractive than that of growth factors because the lectins have not been shown to induce cell mitosis in epithelial cells. That galectin-3 does not induce cell mitosis is further suggested by our findings that the corneal epithelial cell proliferation rate is not perturbed in gal3–/– corneas. Over the last decade, the potential of excimer laser keratectomy to modify the corneal profile for correction of myopia has been realized. Thousands of such procedures are performed each week, providing myopic individuals freedom from eye glasses and contact lenses. In view of the fact that 25–30% of the adult population worldwide is myopic, it has been esti-
mated that nearly half a million such procedures will be performed in the U.S. alone in a given year (45). In some cases following eximer laser surgery, there is a delay in epithelial healing. Such a delay is highly undesirable, because it puts the cornea at risk of developing postoperative haze, infectious keratitis, and ulceration. Again, galectin-based drugs may help promote re-epithelialization of wounds in such cases.

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