Role of JNK-Dependent Serine Phosphorylation of Paxillin in Migration of Corneal Epithelial Cells during Wound Closure

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PURPOSE. Migration of corneal epithelial cells plays an important role in healing of corneal epithelial wounds. The role of c-Jun NH2-terminal kinase (JNK), a member of the family of mitogen-activated protein kinases, in the intracellular signaling responsible for the migration of corneal epithelial cells during wound closure was examined.

METHODS. Scratch wounds were introduced into cultured monolayers of simian virus 40–transformed human corneal epithelial (HCE) cells in the absence or presence of the JNK inhibitor SP600125. The phosphorylation and localization of JNK and paxillin during wound closure were examined by immunoblot and immunofluorescence analyses. The effects of a small interfering RNA (siRNA) specific for JNK and of a mutant form of paxillin on HCE cell migration were determined by transfection.

RESULTS. SP600125 inhibited wound healing in a time- and concentration-dependent manner. Immunoblot analysis showed that wounding increased the phosphorylation of JNK and of paxillin on serine (Ser) 178 in a manner sensitive to SP600125. Immunofluorescence staining revealed that phosphorylated JNK colocalized with paxillin at focal adhesions formed by HCE cells at the wound margin and that SP600125 inhibited the formation of such adhesions. Expression of JNK siRNA or of a paxillin mutant in which Ser178 is replaced by alanine inhibited HCE cell migration during wound closure.

CONCLUSIONS. JNK regulates HCE cell migration by modulating the phosphorylation of paxillin and the consequent formation of focal adhesions. A JNK-paxillin signaling pathway may thus play an important role in corneal epithelial wound healing in vivo.

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The healing of corneal epithelial wounds is important for the maintenance of corneal transparency. Damage to the corneal epithelium induces migration of the remaining epithelial cells to cover the area of the defect; such migration is essential for the initiation of wound healing.1,2 Corneal epithelial cells attach to and migrate over a fibronectin matrix that is deposited in the wound area.3,4 The formation of focal adhesions and reorganization of the actin cytoskeleton play important roles in cell adhesion and migration.5-7 Attachment of corneal epithelial cells to fibronectin induces membrane ruffling as well as the formation of such adhesions and reorganization of the actin network.8,9 We previously showed that inhibition of the formation of focal adhesions results in inhibition of the adhesion and migration of corneal epithelial cells.5 c-Jun NH2-terminal kinase (JNK) is a member of the family of mitogen-activated protein kinases (MAPKs) and has essential roles in a wide variety of cellular processes, including differentiation, apoptosis, and chemotaxis.10-11 Other members of the MAPK family, including extracellular signal-regulated kinase (ERK) and p38 MAPK, have been implicated in corneal epithelial migration.12-15 We have also previously shown that p38 MAPK, but not ERK, contributes to the regulation of corneal epithelial migration by substance P and insulin-like growth factor-1 in the rabbit cornea of organ culture.16 The possible role of JNK in the migration of corneal epithelial cells has remained unknown, however. We have therefore now investigated whether JNK might participate in the regulation of corneal epithelial cell migration during wound closure.

Materials and Methods

Materials

A mixture of Dulbecco modified Eagle medium and nutrient mixture (Nutrient Mixture F-12; DMEM/F-12) as well as reduced serum medium (OPTI-MEM), fetal bovine serum, trypsin-EDTA, gentamicin, and transfection reagent (Lipofectamine 2000) were obtained from Invitrogen-Gibco (Carlsbad, CA). Bovine insulin, cholera toxin, human recombinant epidermal growth factor, nonionic surfactant (Nonidet P-40), and a protease inhibitor cocktail were from Sigma-Aldrich (St. Louis, MO). Plastic 24-well or 60- or 100-mm culture dishes were from Corning (Corning, NY). Inhibitor (SP600125) was obtained from Merck (Whitehouse Station, NJ). Rabbit polyclonal antibodies to JNK were obtained from Cell Signaling (Danvers, MA), those to phosphorylated JNK were from Promega (Madison, WI), and those to paxillin phosphorylated on tyrosine (Tyr) 118 or serine (Ser) 178 were from Abcam (Cambridge, UK) and Biozzi (Montgomery, TX), respectively. A mouse monoclonal antibody to paxillin was obtained from BD Biosciences (Franklin Lakes, NJ). Nuclear staining dye (TOTO-3), fluorescent dye (Alexa Fluor 488)-labeled goat antibodies to rabbit or mouse immunoglobulin G (IgG), fluorescent dye (Alexa Fluor 546)-labeled goat antibodies to mouse IgG, and rhodamine-phalloidin were from Invitrogen. Protein G-Sepharose beads, horseradish peroxidase–conjugated goat secondary antibodies, and enhanced chemiluminescence detection reagents (ECL Plus) were obtained from Amersham Biosciences (Little Chalfont, UK). A small interfering RNA (siRNA) specific for human JNK2 mRNA and a control siRNA were obtained from Santa Cruz Biotechnology (Santa Cruz, CA).

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Cells and Cell Culture

Simian virus 40–immortalized human corneal epithelial (HCE) cells were provided by RIKEN Biosource Center (Tsukuba, Japan). The cells were originally established and characterized by Araki-Sasaki. They were passaged in supplemented hormonal epithelial medium (SHEM), which consists of DMEM/F-12 supplemented with 15% heat-inactivated fetal bovine serum, bovine insulin (5 μg/mL), cholera toxin (0.1 μg/mL), human recombinant epidermal growth factor (10 ng/ml), and gentamicin (40 μg/mL). For experiments, HCE cells were plated at a density of 5 × 10^5 cells per 60-mm dish or 1 × 10^5 cells per well in 24-well plates and were cultured for 48 hours before serum deprivation by incubation in unsupplemented DMEM/F-12 for 24 hours.

Plasmids and Transfection

Plasmids encoding wild-type or S178A mutant (in which Ser178 is replaced by alanine) forms of paxillin were constructed from pGFP-C1 (BD-Clontech, San Jose, CA), which encodes enhanced green fluorescent protein (EGFP), as described previously. HCE cells cultured in 60-mm dishes were transfected for 3 hours with 8 μg plasmid mixed with 20 μL transfection reagent (Lipofectamine 2000; Invitrogen-Gibco) in 5 mL reduced serum medium (OPTI-MEM; Invitrogen-Gibco). The cells were then incubated for an additional 6 hours in SHEM, replated on culture dishes, and cultured for 48 hours before experiments.

Wound Closure Assay

HCE cells cultured in 24-well or 60-mm culture dishes and deprived of serum for 24 hours were incubated for 1 hour with SP600125 or vehicle (0.1% dimethyl sulfoxide [DMSO]) in unsupplemented DMEM/F-12. The cell monolayer was then scraped with the narrow end of a micropipette tip to generate a wound approximately 0.1 cm in width. Phase-contrast images were acquired at various times thereafter with an inverted microscope (Axiovert; Carl Zeiss, Hallbergmoos, Germany) equipped with a charge-coupled device camera (Carl Zeiss). The wound area in each image was determined by computerized planimetry with NIH Image version 1.62f software.

Transfection of siRNA

Cells (5 × 10^5) were seeded in 100-mm dishes and cultured for 24 hours to 50% to 60% confluence. Each siRNA (25 nM) was mixed with 2 μL transfection reagent (Lipofectamine 2000; Invitrogen-Gibco), diluted in 500 μL DMEM, and added to the cells in 4.5 mL reduced serum medium (OPTI-MEM; Invitrogen-Gibco). After incubation with siRNA for 5 hours, the cells were incubated for an additional 6 hours in SHEM, replated on culture dishes, and cultured for 24 hours before experiments.

Immunofluorescence Microscopy

HCE cells cultured on 12-mm coverglasses in 24-well plates and deprived of serum for 24 hours were incubated for 1 hour with inhibitor (SP600125; Merck) or 0.1% DMSO and were wounded as described. At various times thereafter, the cells were fixed for 15 minutes at 37°C with 3.7% formalin, washed with Ca^2+ - and Mg^2+-free phosphate-buffered saline (PBS−), permeabilized for 5 minutes with 0.1% Triton X-100 in PBS−, and incubated for 1 hour at room temperature with 1% bovine serum albumin (BSA) in PBS−. They were then incubated for 1 hour with antibodies to paxillin and to phospho-JNK, each at a dilution of 1:100 in PBS− containing 1% BSA, washed with PBS−, and incubated for 1 hour with corresponding fluorescent dye (Alexa Fluor; Invitrogen)–conjugated secondary antibodies (1:1000 dilution in PBS− containing 1% BSA), rhodamine-phalloidin (1:200 dilution in PBS− containing 1% BSA), and nuclear staining dye (TOTO-3; Invitrogen; 1:1000 dilution in PBS− containing 1% BSA). Finally, they were examined with a laser confocal microscope (LSM5; Carl Zeiss).

Immunoblot Analysis

HCE cells cultured in 60-mm dishes and wounded as described were lysed on ice in 0.5 mL solution containing 50 mM Tris-HCl (pH 7.5), 150 mM NaCl, 1 mM EDTA, 5 mM NaF, 1% nonionic surfactant (Nonidet P-40; Sigma-Aldrich), 0.5% sodium deoxycholate, 0.1% sodium dodecyl sulfate (SDS), 1 mM Na_2VO_3, and 1% protease inhibitor cocktail. The lysates were centrifuged at 15,000g for 15 minutes at 4°C, and the resultant supernatants (20 μg protein) were subjected to SDS-

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**Figure 1.** Inhibition of HCE cell migration by inhibitor (SP600125) in an in vitro model of corneal epithelial wound healing. (A) Confluent monolayers of HCE cells were deprived of serum for 24 hours, incubated for 1 hour with 10 μM inhibitor (SP600125) or vehicle (0.1% DMSO), and subjected to scratch wounding. The cells were fixed immediately or 24 hours after wounding, and the wounded area of the cell monolayer was examined by phase-contrast microscopy. (B) HCE cells were treated with various concentrations of inhibitor (SP600125) and were wounded as in (A), and the remaining area of the wound was determined at the indicated times thereafter. Data are mean ± SE of triplicates from an experiment that was repeated three times with similar results. *P < 0.05 versus corresponding value for cells treated with 0.1% DMSO (0 μM inhibitor (SP600125)).
polycrylamide gel electrophoresis on a 10% gel. Separated proteins were transferred to a nitrocellulose membrane, which was then exposed to 5% skim milk for 1 hour at room temperature before incubation for 1 hour with primary antibodies at a dilution of 1:1000 in washing buffer (20 mM Tris-HCl [pH 7.4], 5% skim milk, 0.1% Tween 20). The membrane was washed in washing buffer, incubated for 1 hour at room temperature with horseradish peroxidase–conjugated secondary antibodies (1:1000 dilution in washing buffer), washed again, incubated with enhanced chemiluminescence (ECL Plus; Amersham Biosciences) detection reagents for 5 minutes, and exposed to film.

**Immunoprecipitation Assay**

HCE cells were cultured in 60-mm dishes, deprived of serum for 24 hours, incubated for 1 hour with 10 μM inhibitor (SP600125; Merck) or 0.1% DMSO in unsupplemented DMEM/F-12, and scraped as described. After 15 minutes, the cells were lysed on ice in 0.5 mL solution containing 50 mM Tris-HCl (pH 7.5), 100 mM NaCl, 2 mM MgCl₂, 10% glycerol, 1 mM EGTA, 1 mM NaF, 1% nonionic surfactant (Nonidet P-40; Sigma-Aldrich), 100 μM Na₃VO₄, and 1% protease inhibitor cocktail. The lysates were centrifuged at 15,000 g for 10 minutes at 4°C, and portions of each supernatant (100 μg protein) were incubated for 16 hours at 4°C in a final volume of 200 μL with antibodies to paxillin (1:100 dilution) and 20 μL Protein G–Sepharose beads. The beads were isolated by centrifugation and washed twice with cell lysis solution, and the bound proteins were subjected to immunoblot analysis, as described.

**Statistical Analysis**

Quantitative data are presented as mean ± SE. Differences were analyzed with Dunnett test. P < 0.05 was considered statistically significant.

**RESULTS**

We examined the possible role of JNK in corneal epithelial migration during wound closure with the use of an in vitro model in which a monolayer of HCE cells was subjected to a scratch wound. HCE cells were cultured for 48 hours to generate a confluent monolayer, deprived of serum for 24 hours, and exposed to the JNK inhibitor (10 μM; SP600125; Merck) or vehicle (0.1% DMSO) for 1 hour before wounding. Cells were fixed 24 hours after wounding; and the wounded area was examined by phase-contrast microscopy. Although the cells incubated with vehicle had migrated into and largely covered the original wound area, those incubated with inhibitor (SP600125; Merck) failed to cover a substantial portion of the wound (Fig. 1A). Quantitation of the remaining wound area revealed that the inhibitor (SP600125; Merck) inhibited HCE cell migration in a time- and concentration-dependent manner (Fig. 1B). Although the cells incubated with vehicle covered approximately 80% and 90% of the original wound area after 12 and 24 hours, respectively, those incubated with 30 μM inhibitor (SP600125; Merck) covered only approximately 30% and 50% of the wound area at these times. These results thus suggested that JNK plays a role in wounding-induced HCE cell migration.

We next investigated changes in the morphology of HCE cells apparent at the wound margin 12 hours after wounding. Immunofluorescence analysis with antibodies to paxillin revealed numerous small dotlike structures, presumably corresponding to focal adhesions, that were associated with membrane ruffles and bundles of F-actin in control cells exposed to vehicle (Fig. 2). In contrast, cells treated with 10 μM inhibitor (SP600125; Merck) exhibited only a thin rim of F-actin staining and only a few small dotlike structures containing paxillin immunoreactivity at the cell periphery. These results suggested that JNK activation is required for the formation of lamellipodia ruffles and focal adhesions by HCE cells at the wound margin.

We next examined whether JNK is indeed activated in response to wounding of HCE cell monolayers. Immunoblot analysis of control cells treated with vehicle revealed a marked and transient increase in the amount of phosphorylated (activated) JNK that was apparent 5 and 15 minutes after wounding, with the level of JNK phosphorylation returning to baseline values by 30 minutes (Fig. 3). In contrast, this response was greatly attenuated in cells treated with 10 μM inhibitor (SP600125; Merck). The total amount of JNK was not affected...
by wounding in cells treated with vehicle or inhibitor (SP600125; Merck).

To confirm the specificity of the observed effects of inhibitor (SP600125; Merck), we also examined the effects of depletion of endogenous JNK in HCE cells by RNA interference. We transfected HCE cells with an siRNA specific for JNK or with a control siRNA and then cultured the cells for 48 hours before determining the amount of JNK. Immunoblot analysis of cells transfected with the JNK siRNA revealed a marked decrease in the abundance of JNK compared with that in cells transfected with the control siRNA (Fig. 4A). Migration of HCE cells in the wound closure assay was also inhibited in a time-dependent manner by transfection with the JNK siRNA (Fig. 4B). Although cells transfected with the control siRNA covered approximately 60% and 80% of the original wound area after 12 and 24 hours, respectively, those transfected with the JNK siRNA covered only approximately 30% and 70% of the wound area at these times. We also examined the morphology of JNK-depleted HCE cells at the wound margin 12 hours after wounding. Immunofluorescence analysis revealed that the effects of transfection with the JNK siRNA (Fig. 5A) were virtually identical with those of inhibitor (SP600125; Merck; Fig. 2). Furthermore, immunoblot analysis confirmed that JNK phosphorylation in response to wounding was greatly decreased in HCE cells transfected with JNK siRNA compared with that apparent in cells transfected with control siRNA (Fig. 5B).

We examined the localization of phosphorylated JNK in HCE cells by immunofluorescence analysis 15 minutes after wounding (Fig. 6A). Staining corresponding to phosphorylated JNK was markedly increased in cells at the wound margin of monolayers treated with vehicle compared with that apparent in those treated with 10 μM inhibitor (SP600125; Merck). The

**FIGURE 4.** Effect of JNK depletion by RNA interference on HCE cell migration during wound healing. (A) Cells were transfected with an siRNA specific for JNK mRNA (25 nM) or with a control siRNA (25 nM), cultured for 48 hours, and subjected to immunoblot analysis with antibodies to JNK or to actin (loading control). (B) Cells transfected as in (A) were wounded as in Figure 1, and the remaining area of the wound was determined at the indicated times thereafter. Data are mean ± SE of values from three independent experiments. *P < 0.05 versus corresponding value for cells transfected with the control siRNA.

**FIGURE 5.** Effects of JNK depletion by RNA interference on cell morphology at the wound margin and on JNK phosphorylation in HCE cells. (A) Cells were transfected with JNK or control siRNA and subjected to scratch wounding, as in Figure 4B, were fixed 12 hours after wounding, permeabilized, and subjected to staining for F-actin (red) with rhodamine-phalloidin, for paxillin with specific antibodies (green), and for nuclei with nuclear staining dye (blue). Scale bar, 20 μm. Data are representative of three independent experiments. (B) Cells were transfected with JNK or control siRNA and subjected to scratch wounding, were cultured for the indicated times, after which cell lysates were subjected to immunoblot analysis with antibodies to phosphorylated JNK. Data are representative of three independent experiments.
staining colocalized to a large extent with paxillin immunoreactivity at putative focal adhesions, which was also increased in the cells exposed to vehicle compared with that in cells exposed to 10 μM inhibitor (SP600125; Merck). We also examined whether the association between paxillin and JNK could be detected by immunoprecipitation with antibodies to paxillin. Immunoblot analysis of immunoprecipitates prepared from vehicle-treated control cells 15 minutes after wounding revealed that endogenous paxillin interacted with endogenous JNK (Fig. 6B); in contrast, this association was greatly inhibited in cells treated with 10 μM inhibitor (SP600125; Merck).

In addition, we examined whether paxillin was phosphorylated during wound closure. Immunoblot analysis with antibodies to the phosphoserine-178 form of paxillin revealed a marked increase in the amount of paxillin phosphorylated on this residue as early as 5 minutes after wounding in control cells treated with vehicle; the level of Ser178 phosphorylation also remained increased at 60 minutes in these cells (Fig. 7). In contrast, wounding failed to increase the amount of paxillin phosphorylated on Ser178 in cells treated with 10 μM inhibitor (SP600125; Merck). HCE cells manifested constitutive phosphorylation of paxillin on Tyr 118, and such phosphorylation was not affected by wounding or by inhibitor (SP600125; Merck). The total amount of paxillin in HCE cells was also not affected by wounding or this drug. These findings thus suggested that the activation of JNK was required for the phosphorylation of paxillin on Ser178 during wound closure.

We examined the role of paxillin phosphorylation on Ser178 in wound closure with HCE cells transfected with an expression vector for an EGFP-tagged mutant form of paxillin (Ser178Ala) in which this residue is replaced with alanine. The rate of wound closure was significantly reduced in cells expressing this mutant protein compared with that apparent in cells expressing EGFP-tagged wild-type paxillin or EGFP alone (Fig. 8). Finally, we determined the localization of the EGFP-tagged mutant (Ser178Ala) and wild-type forms of paxillin after wounding by immunofluorescence analysis. Both EGFP-tagged proteins localized to focal adhesions at the wound margin (Fig. 9).

**DISCUSSION**

We have shown that JNK was activated in HCE cells during wound closure in vitro and that a JNK inhibitor markedly inhibited HCE cell migration during wound closure in a time-dependent manner.
and concentration-dependent manner. Depletion of endogenous JNK by RNA interference also inhibited HCE cell migration during wound closure. Furthermore, phosphorylated JNK was found to co-localize with paxillin at putative focal adhesions formed by HCE cells at the wound margin, and JNK was shown to interact with paxillin by immunoprecipitation analysis. The JNK inhibitor also blocked lamellipodia associated with the formation of focal adhesions and the interaction between JNK and paxillin. Phosphorylation of paxillin on Ser178 was induced by wounding of HCE cell monolayers in a manner sensitive to the JNK inhibitor, and expression of the Ser178Ala mutant form of paxillin inhibited cell migration during wound closure. These results implicate JNK-paxillin signaling in the regulation of HCE cell migration associated with wound closure.

Our observation that the JNK inhibitor (SP600125; Merck) inhibited HCE cell migration during wound closure is consistent with the previously observed effects of this inhibitor on keratinocytes and bladder epithelial cells.19,20 Mice that lack JNK also exhibit defects in closure of the embryonic optic fissure and eyelid closure.21,22 Furthermore, the kinase MEKK1, an upstream activator of JNK signaling, has been implicated in eyelid closure, corneal development, and corneal epithelial migration.23,24 These observations suggest that the activation of JNK is a central event in the migration of corneal epithelial cells. In contrast, hepatocyte growth factor and keratinocyte growth factor were each shown to promote the migration of rabbit corneal epithelial cells in primary culture through the activation of p38 MAPK and ERK but not through that of JNK.13 In our experimental system, wound closure was studied in the absence of growth factors. The response of the cells to wounding was thus mediated entirely by endogenous components. These results suggest that the regulation of corneal epithelial cell migration by members of the MAPK family of proteins might be context dependent.

Paxillin regulates the formation of focal adhesions and contributes to cell migration.25,26 We found that phosphorylated JNK colocalized with paxillin at presumptive focal adhesions formed by HCE cells at the wound margin, and that the phosphorylation of paxillin on Ser178 during cell migration was dependent on JNK activation. Immunoprecipitation analysis confirmed the interaction between JNK and paxillin during wound closure. Moreover, the JNK inhibitor greatly inhibited the formation of focal adhesions and the interaction between JNK and paxillin during wound closure. These results suggest that JNK may interact with and phosphorylate paxillin and

**FIGURE 8.** Inhibition of HCE cell migration during wound closure by expression of the Ser178Ala mutant form of paxillin. Cells were transfected with plasmids encoding EGFP alone or EGFP-tagged wild-type or Ser178Ala mutant forms of paxillin. Cell monolayers were subsequently deprived of serum for 24 hours and wounded, and the extent of wound closure was determined 0, 12, or 24 hours thereafter, as described for Figure 1. Data are mean ± SE of values from three separate experiments. *P < 0.05 versus the corresponding value for cells transfected with the control vector for EGFP alone.

**FIGURE 9.** Localization of Ser178Ala mutant and wild-type forms of paxillin in HCE cells at the wound margin. Cells were transfected with plasmids encoding EGFP-tagged wild-type or S178A mutant forms of paxillin and wounded as in Figure 8. Twelve hours thereafter, the cells were stained for F-actin (red) with rhodamine-phalloidin and for nuclei with nuclear staining dye (blue). The green fluorescence of EGFP was also monitored. Scale bar, 10 μm. Data are representative of three independent experiments.
thereby regulate the formation of focal adhesions in and the migration of HCE cells. Tyrosine phosphorylation of paxillin has also been implicated in cell spreading and migration.\textsuperscript{25,26} Previous studies have shown that the tyrosine phosphorylation of paxillin is upregulated during the migration of corneal epithelial cells and contributes to the migration of these cells.\textsuperscript{27–29} In the present study, however, though paxillin phosphorylation on Ser178 was induced by wounding of HCE cell monolayers in a manner dependent on JNK activation, paxillin phosphorylation on Tyr118 was not affected by wounding or by the JNK inhibitor. Consistent with these results, expression of the Ser178Ala mutant of paxillin inhibited HCE cell migration during wound closure. These observations suggest that JNK mediates the phosphorylation of paxillin on Ser178 and that paxillin phosphorylation on this residue is required for HCE cell migration during wound closure. Paxillin phosphorylation on Tyr118 might also be necessary for HCE cell adhesion and migration but is constitutive.

Although the Ser178Ala mutant of paxillin inhibited HCE cell migration during wound closure, the overexpression of wild-type paxillin had no effect on this process. This latter observation might be explained if the abundance of endogenous paxillin is not limiting for HCE cell migration. Both the Ser178Ala mutant and the wild-type forms of paxillin localized to focal adhesions formed by HCE cells at the wound margin. The Ser178Ala mutant and the wild-type forms of paxillin were previously shown to localize to focal adhesion–like structures in bladder epithelial cells.\textsuperscript{30} Whether the association of the Ser178Ala mutant with focal adhesions proteins differs from that of the wild-type protein in HCE cells remains to be determined.

Activation of the small GTPase Rho induces the assembly of actin stress fibers and promotes the formation of focal adhesions.\textsuperscript{31,32} whereas activation of the Rho family proteins Rac and Cdc42 elicits the formation of lamellipodia or the formation of filopodia, respectively.\textsuperscript{33} Rac and Cdc42 also induce the assembly of small focal adhesions, termed focal contacts.\textsuperscript{34} We previously showed that fibronectin activates Rac1 and induces the formation of lamellipodia and focal adhesions, resulting in increased cell adhesion and motility, in HCE cells.\textsuperscript{9} These previous observations and our present observations thus suggest that JNK likely functions downstream of Rho family proteins in the regulation of HCE cell migration during wound healing.

In conclusion, our present results implicate a JNK-paxillin signaling pathway in the regulation of HCE cell migration during wound closure. Further characterization of the mechanism of this regulation may provide a better understanding of corneal epithelial wound healing and a basis for the development of new treatments for corneal epithelial wounds.

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