Kruppel-like Factor 4 Regulates Laminin α3A Expression in Mammary Epithelial Cells*

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The laminin family of extracellular matrix glycoproteins is heterotrimeric proteins consisting of three distinct subunits, designated α, β, and γ that are encoded by the LAMA, LAMB, and LAMC genes, respectively. To date there are five α chains, three β chains, and two γ chains that assemble into 12 laminins. Laminin-5 (α3A, β3, and γ2) is the major extracellular matrix protein produced in mammary epithelial cells. In these cells laminin-5 functions as a ligand for the α9β1 and α9β4 integrins to regulate adhesion, migration, and morphogenesis (1). Loss of laminin-5 has been found in breast cancer progression. Henning et al. (2) demonstrated a loss of laminin-5 protein expression by immunostaining in malignant lesions while benign ductal and lobular proliferations and fibroadenomas show continuous laminin-5 staining at the epithelial-stromal interface. Martin et al. (3) used a molecular approach to analyze mRNA expression of the laminin-5 subunits and found no expression in late stage tumors and decreased expression in early stage tumors compared with normal breast epithelial cells.

The murine LAMA3A promoter has been studied and found to contain three binding sites for the complex dimeric transcription factor, AP-1, one site of which is essential for basal expression of LAMA3A in keratinocytes (4). Mutation of this single key AP-1 site reduced promoter activity by ~90% while mutation of the other two sites had much less effect (4). In the present study we analyze the human LAMA3A promoter in the MCF10A mammary epithelial cell line and the T47D breast cancer cell line. We sought to find a mechanism that would explain the LAMA3A down-regulation in the nonexpressing cells. In doing this, we demonstrated a key role for the transcription factor Kruppel-like factor 4 (KLF4)† in regulating this gene.

KLF4, also known as gut-enriched Kruppel-like factor (GKLF) and epithelial zinc finger (EZF), is a member of the Kruppel-type zinc finger transcription factors (5–8). One of the best known members of this family is the erythroid Kruppel-like factor that is involved in the activation of the β-globin promoter in red blood cells (9). The family also includes KLF1 (10), KLF11 (11), IKLF (12), BTEB2 (13), and BKL (14), many of which are tissue specific in their expression. Members of the Kruppel-type family are highly conserved in the carboxyl-terminal region that contains three zinc fingers and they bind similar GC-rich recognition sequences. KLF4 is a nuclear protein shown to contain both transcriptional activation and repression domains (8). In keratinocytes, KLF4 activates the keratin 4 promoter and may be important in the transition toward differentiation (7). KLF4 has also been shown to be involved in the regulation of the CYP1A1 gene (15). This report describes the novel role of this factor in the regulation of the LAMA3A promoter. Through transient transfections and EMSA we show that KLF4 activates expression of the LAMA3A gene in MCF10A cells and that loss of KLF4 activity is in part responsible for the loss of LAMA3A expression in breast cells.

EXPERIMENTAL PROCEDURES

Cell Culture and Transfections—MCF10A (a nontransformed, spontaneously immortalized human breast epithelial cell line) and M-H cells (a hygromycin resistant subclone of MCF10A cells) were maintained as previously described (16). T47D cells were cultured in RPMI 1640

†The abbreviations used are: KLF4, Kruppel-like factor 4; GKLF, gut-enriched Kruppel-like factor; EZF, epithelial zinc finger; EMSA, electrophoretic mobility shift assay.

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The nucleotide sequence(s) reported in this paper has been submitted to the GenBank®/EBI Data Bank with accession number(s) AF279435.

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medium supplemented with 0.01 mg/ml insulin and 10% heat inactivated fetal bovine serum. MDA-MB 231, MCF7, and ZR75-1 cells were cultured in RPMI 1640 medium supplemented with 10% fetal bovine serum and 300 μg/ml glutamine. MDA-MB 436 cells were cultured in RPMI 1640 medium supplemented with 10% fetal bovine serum, 0.01 mg/ml insulin, 0.15 mg/ml CA, 10 mM MgCl₂, and 13 mM T4T12 and transfected in log growth phase at a density of 1 × 10⁶ cells per well in 6-well plates using the Superfect Transfection Reagent (Qiagen, Inc.) per the manufacturer’s protocol. Quantities transfected of the respective vectors are indicated in the figure legends. Cells were harvested in Reporter Lysis Buffer (Promega Corp.) between 24 and 48 h. Luciferase activity was assayed by mixing aliquots of cell extracts with luciferin reaction mixture (Promega Luciferase Assay Kit) and emission of light was quantitated with a Microlumat luminometer.

Probes A. Labeled probes were then separated from free [α-32P]dCTP using Sephadex ProbeQuant G-50 micro columns (Amersham Pharmacia Biotech). Binding reactions included: [α-32P]-labeled DNA probes (1–5 ng, 100,000 cpm); 4 μg of poly(dC-dC); 10 μg of nuclear extract; 5 μg of bovine serum albumin; 8 μl of 5 × binding buffer (50 mM HEPES pH 7.9, 5 mM dithiobitol, 0.5% Triton X-100, and 2.5% glycerol); and the appropriate volume of H₂O to a final volume of 30 μl. Binding reaction mixtures were then incubated at 30 °C for 30 min. Bound products were resolved by electrophoresis through a 7% or 8% native polyacrylamide gel in 1 × running buffer (50 mM Tris, 0.38 μg/ml glycerol, 2.0 mM EDTA, pH 8.5). Gels were dried with a Bio-Rad Gel Dryer for 45 min at 85°C, followed by exposure to Hyperfilm-MP (Amersham Pharmacia Biotech) at −70 °C. Film was then developed using an x-ray film processor (Fuji).

To deplete extracts of KLF4, 50 μl of nuclear extracts from an MCF10A subclone were incubated for 4 h at 4 °C with either 20 μl of rabbit preimmune serum or 10 μl each of KLF4 antibodies from Dr. Yang (6) and Dr. Tseng (18) and 40 μl of protein G-agarose beads (Life Technologies). Samples were briefly centrifuged, and supernatants were washed with gel shifts and used in the binding reactions.

Competition experiments consisted of 150 × molar excess for the TDA, AP-1, and AP2 oligonucleotides that were preincubated with nuclear extracts for 30 min at room temperature before proceeding to the binding reactions with the 103-base pair DNA fragment. AP-1 and AP2 duplex oligonucleotides were obtained from Stratagene, the AP2 oligonucleotide serving as a nonspecific control. Competition of the labeled TDA probe consisted of 125 × molar excess of TDA(WT) and TDA(M6-mut) oligonucleotides in Fig. 6A and 250 × molar excess in Fig. 6B.

Western Analysis—Cells were lysed in RIPA buffer (50 mM Tris, pH 8.0, 150 mM NaCl, 1% Nonidet P-40, 0.05% deoxycholic acid, 1% SDS, 1 mM EDTA, 20 μg/ml phenylmethylsulfonyl fluoride, 1 μg/ml pepstatin, 1 μg/ml leupeptin, 1 μg/ml aprotinin). Protein concentrations were determined using the Bio-Rad protein reagent assay, 40 μg of protein were electrophoresed by SDS-polyacrylamide gel electrophoresis, transferred to nitrocellulose, and blotted using the rabbit polyclonal anti-KLF4 antibody (Santa Cruz Biotechnology, Santa Cruz, CA). Goat anti-rabbit HRP (Bio-Rad Laboratories) was used as a secondary antibody and detected using ECL reagent (Amersham Pharmacia Biotech).

RESULTS

The a3 Subunit of Laminin-5 Is Not Expressed in Breast Cancer Cell Lines—There is previous evidence that laminin-5 is down-regulated in breast cancer cell lines. Examination of mRNA in breast tumor cells showed that laminin a3 was greatly reduced or not present at all in breast tumor tissue and 15 breast cancer cell lines including T47D, MCF7, ZR75-1, MDAMB 436, BT474, MDA-MB 361, and MDA-MB 231 (3). Long exposure of Northern blots revealed very low level expression in breast cancer cell lines, ruling out systematic deletion of this gene in breast cancer (3). The main transcript of the laminin-5 a3 subunit in mammary epithelia is the LAMA3A isoform (19). In the mouse the genetic structure of the mLAMA3A gene consists of the mLAMA3A and mLAMA3B isoforms that each contain a unique exon 1 that is expressed using alternative promoters. Exon 1 of mLAMA3B is upstream of the mLAMA3A exon and the intron region between these exons contains an Alu repeat. The Quick Change Mutagenesis Kit from Stratagene was used to create site-directed mutants of the full-length pl3A vector. An oligonucleotide that changes overlapping KLFP-binding sites starting at base pair −412 from 5'-CTTCCCTCCCTCTC-3' to 5'-CTTCCCTTTCAGCCCCACTTCT-3' created mutation p3A-KLF4mut1. p3A-KLF4mut2 changes the KLFP site at −387 from 5'-GAGGGAAAAGAGGAGG-3' to 5'-GAGGGAAAAAGGATCT-3'. The mutation KLFPmut3 changes the binding site at base pair 1865 from 5'-GCTGACTCATG-3' to 5'-GCTGACTTATG-3'. This corresponds to the AP-1B site described in the mouse promoter by Virolle et al. (28).

The overexpression of tissue transglutaminase in breast cancer cell lines was used to verify the correct mutations were created. EMSA—Nuclear extracts were prepared by collecting cells in cold Buffer A (10 mM HEPES pH 7.9, 1.5 mM MgCl₂, 10 mM KCl, 0.5 mM diithiothreitol, 0.2 mM phenylmethylsulfonyl fluoride) and incubated on ice for 10 min. Cells were then frozen and thawed once and vortexed for 10 s. Nuclei were pelleted by brief centrifugation and resuspended in cold Buffer C (20 mM HEPES pH 7.9, 25% glycerol, 420 mM NaCl, 1.5 mM MgCl₂, 0.2 mM EDTA, 0.5 mM dithiothreitol, 0.2 mM phenylmethylsulfonyl fluoride), incubated for 30 min, briefly centrifuged to remove debris, and the nuclear extract supernatant was collected and used at −70 °C. Primers to the p3A vector were used to amplify probe A, the 103-base pair fragment spanning bases −199 to −97, for gel shift analysis, 5'-CGGCTCTGGCCAGGG-3' to 5'-TCTGCTGCTAGTCGG-3'. Probe A was radiolabeled with [α-32P]dCTP (Amersham Pharmacia Biotech) using T4 polynucleotide kinase. Probe B (−84 to −62) was created by annealing two oligonucleotides, 5'-AGAGGAGGAGGCA-GAGGTTCC-3' and 5'-CAGGAGAAGCTTCAGTTCTCTTCTC-3', that contain base pair overhangs that were radiolabeled using DNA polymerase in the presence of [α-32P]dCTP (Amersham Pharmacia Biotech). The oligonucleotide containing the KLFP consensus sequence designated TDA by Shields and Yang (15) and an oligonucleotide based on the TDA with 2 base pair mismatches described above and KLFP designated TDAmut were created as described by Shields and Yang (17) and end labeled as Probe A. Labeled probes were then separated from free [α-32P]dCTP using Sephadex ProbeQuant G-50 micro columns (Amersham Pharmacia Biotech). Binding reactions included: [α-32P]-labeled DNA probes (1–5 ng, 100,000 cpm); 4 μg of poly(dC-dC); 10 μg of nuclear extract; 5 μg of bovine serum albumin; 8 μl of 5 × binding buffer (50 mM HEPES pH 7.9, 5 mM dithiothreitol, 0.5% Triton X-100, and 2.5% glycerol); and the appropriate volume of H₂O to a final volume of 30 μl. Binding reaction mixtures were then incubated at 30 °C for 30 min. Bound products were resolved by electrophoresis through a 7% or 8% native polyacrylamide gel in 1 × running buffer (50 mM Tris, 0.38 μg/ml glycerol, 2.0 mM EDTA, pH 8.5). Gels were dried with a Bio-Rad Gel Dryer for 45 min at 85°C, followed by exposure to Hyperfilm-MP (Amersham Pharmacia Biotech) at −70 °C. Film was then developed using an x-ray film processor (Fuji).

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KLF4 Regulates LAMA3A Expression—The murine LAMA3A promoter contains three AP-1 sites (AP-1A, AP-1B, and AP-1C) that are involved in the up-regulation of this gene by transforming growth factor-β in keratinocytes (4). One of these sites, designated AP-1-B is critical for basal expression as determined to be the USF site. Data represent at least two experiments performed in triplicate. Error bars represent standard error. B, transient transfection of pL3A mutant vectors in MCF10A cells. 1 μg of each vector was co-transfected with 200 ng of cytomegalovirus-β-galactosidase vector. Transfections were normalized to β-galactosidase activity. MCF10A cells contain high LAMA3A promoter activity, while T47D cells have very low expression. Data represents at least two experiments performed in triplicate. Error bars represent standard error.

FIG. 1. Control of LAMA3A by KLF4 and AP-1. A, expression of LAMA3A is decreased in breast cancer cells. Transient transfection of 1 μg of the pL3A vector containing the human LAMA3A promoter in the pGL2 basic vector was compared with transfection of 1 μg of pGL2 basic vector in MCF10A and T47D cells. All wells were transfected with 200 ng of a cytomegalovirus-β-galactosidase vector. Transfections were normalized to β-galactosidase activity. MCF10A cells contain high LAMA3A promoter activity, while T47D cells have very low expression. Data represents at least two experiments performed in triplicate. Error bars represent standard error. B, transient transfection of pL3A mutant vectors in MCF10A cells. 1 μg of each vector was co-transfected with 200 ng of cytomegalovirus-β-gal. Luciferase counts were normalized to β-galactosidase activity. MCF10A cells contain high LAMA3A promoter activity, while T47D cells have very low expression. Data represents at least two experiments performed in triplicate. Error bars represent standard error.
KLF4 Regulates LAMA3A Expression

**FIG. 3.** KLF4 is expressed in MCF10A but not MCF7, T47D, or MDA-MB 231 breast cancer cells. Forty micrograms of whole cell extract from MCF-7 (lane 1), MCF10A (lane 2), T47D (lane 3), and MDA-MB 231 (lane 4) cells were electrophoresed by SDS-polyacrylamide gel electrophoresis, transferred to nitrocellulose and blotted with KLF4 antibody (Santa Cruz Biotechnology) at a dilution of 1:1000.

**FIG. 4.** Tumor cell lines lack KLF4 transcriptional activity. LAMA3A nonexpressing cells have less KLF4 transcriptional activity. Transient transfection of 5 μg of TDA/WTx2-pGL2-TATA-Luc (black bars) or TDA/M6-Mut x2-pGL2-TATA-Luc (gray bars) in MCF10A and T47D cells. Data represent two experiments performed in triplicate. Error bars show standard error.

KLF4 Activity Is Decreased in Breast Cancer Cells—To further confirm the lack of KLF4 protein in the breast cancer cells, we compared general KLF4 activity of MCF10A to the activity of T47D cells. Shields and Yang (17) have published a consensus binding sequence for KLF4. The vector TDA/WTx2-pGL2-TATA-Luc basic contains two tandem copies of this consensus sequence upstream of a TATA element in the pGL2 basic vector. This vector has been shown to be activated by KLF4 (17). The TDA/M6-Mut x2-pGL2-TATA-Luc vector has mutations in the KLF4 consensus and is not KLF4 responsive. We tested activity of the TDA/WT vector compared with the TDA/M6-Mut vector to analyze the overall KLF4 transcriptional activity in MCF10A and T47D cells. When the TDA vector was transfected in MCF10A cells, there was a 6-fold increase in transcriptional activity compared with the mutant vector that does not bind KLF4 (Fig. 4). Activation in the T47D cells, on the other hand was negligible (Fig. 4). We next analyzed KLF4 DNA binding activity by EMSA in MCF10A and five different breast cancer cell lines. An oligonucleotide for EMSA analysis was created that contained the TDA consensus sequence as previously described (17). We found specific binding to the TDA-labeled oligonucleotide that was competed with cold TDA oligonucleotide but not the TDA mutant oligonucleotide in MCF10A cells (Fig. 5A). Specific binding was lacking in the five...
breast cancer cell lines tested (Fig. 5A). The competition in Fig. 5A was at 125 \times H11003 molar excess that did not completely compete the TDA oligonucleotide. In Fig. 5B the competition was performed at 250 \times H11003 molar excess that demonstrated complete complex inhibition with TDA(WT) but not TDA(Mut) oligonucleotides in MCF10A cells. The high level of competitor required for competition of binding to the labeled TDA oligonucleotide suggested a high level of KLF4 DNA binding activity in MCF10A cells. These data demonstrated that the KLF4 transcriptional activity and DNA binding activity was greater in the MCF10A cells than the breast cancer cells.

Expression of KLF4 in Breast Cancer Cells Stimulates LAMA3A Transcription—Lack of KLF4 protein expression and activity in breast cancer cells lead us to hypothesize that expressing KLF4 in the breast cancer cells would have a positive effect on pL3A activity in these cells. Expression of the pL3A vector was increased 15-fold in T47D cells when co-transfected with 10 ng of the pcDNA3-hEZF vector obtained from Dr. Mu-En Lee (8) (Fig. 6B). In MDA-MB-231 cells (Fig. 6C) the fold induction with 10 ng of pcDNA3-hEZF was 39-fold the basal expression of pL3A in these cells and in MCF7 cells (Fig. 6D) the induction was 20-fold. Thus, expression of KLF4 alone was sufficient to see promoter activity in LAMA3A nonexpressing cells. Transfection of the plasmids with mutated KLF4-binding sites into MCF7 cells (pL3A-Mut5 and pL3A-Mut6) showed no activation in the presence of co-transfected KLF4 (data not shown). We were unsure what the results would be of overexpressing KLF4 in the MCF10A cells that already express KLF4 protein. Co-transfection of pL3A with low doses of the pcDNA3-hEZF vector in MCF10A cells resulted in an increase in luciferase activity (Fig. 6A). On the other hand, a higher dose of KLF4 in MCF10A cells resulted in repression of the promoter by about 5-fold, suggesting that optimal levels of KLF4 are necessary for LAMA3A expression.

DISCUSSION

Laminin-5 is a highly tissue-specific gene with expression found only in epithelial cell populations. A recent study shows that the human LAMA3A promoter is also driven by AP-1 (22). Virolle et al. (22) suggest that the conformation of the AP-1 sites is critical in determining whether LAMA3A expression occurs or not. They suggest that under normal circumstances, a repressor binds AP-1 in the fibroblasts but this repressor is absent in keratinocytes which allows expression of LAMA3A. Our results confirm a role of AP-1 in the regulation of the human LAMA3A promoter. Mutation of the AP-1 site decreases transcriptional activity of pL3A in MCF10A cells. Unlike the previous report, our gel shift analysis does not suggest the
The presence of a repressor complex that is unique to the breast cancer cells. Instead we find that the presence of KLF4 is involved. In MCF10A cells that contain KLF4, mutation of KLF4-binding sites also results in decreased transcription of pL3A. We show that breast cancer cells lack KLF4 expression and activity which likely results in the lack of LAMA3A expression in these cells. Expression of the LAMA3A promoter in the breast cancer cells by expression of KLF4 further supports this claim. This is not the first time that KLF4 has been shown to be involved in tissue specific expression. Presence of KLF4 has been shown to confer tissue specific expression of keratin 19 in pancreatic ductal cells (23). Aciar cells that do not express keratin 19 lack KLF4. We suggest that like keratin 19, LAMA3A expression relies on the presence of KLF4; cells that express KLF4 will express LAMA3A and those that do not express KLF4 will not express LAMA3A.

These studies do not address the mechanism of loss of KLF4 in the breast cancer cells. Further analysis is necessary to determine whether lack of KLF4 is due to gene loss, transcriptional repression, or protein instability. Studies in colon cells suggest that transcription of KLF4 is reduced in cancer cells. It has been shown that KLF4 mRNA is decreased in colon cancer cells and has an effect on the proliferation and differentiation of these cells (24, 25). Dang et al. (26) find that expression of KLF4 is decreased in patients with familial adenomatous polyposis. The actual regulation of KLF4 is not very well understood at this time. Several factors including Cdx2, Sp1, Sp3, and KLF4 itself may be involved in its regulation (27).

Higher doses of KLF4 results in declining LAMA3A promoter activation in both MCF10A and cancer cells. The mechanism for this is unknown. KLF4 has been shown to have both activation and repression domains (8). Also, the Cyclin D1 promoter has been shown to be repressed by KLF4 by competing away the positive acting transcription factor SP1 (18). Further studies will be necessary to determine the mechanism by which large amounts of KLF4 can result in inhibition of LAMA3A transcription.

It is unclear whether AP-1 and KLF4 form a complex in MCF10A cells. In the gel shift of Probe A which contains both AP-1- and KLF4-binding sites, we see that an AP-1 competitor competes only the AP-1 band while a KLF4 competitor competes both the AP-1 and KLF4 bands. However, there is no effect on AP-1 binding with the KLF4 oligo in the breast cancer cells. It is possible that the competition of AP-1 in the MCF10A cells with KLF4 is due to an interaction of the two transcription factors. Further studies would be necessary to confirm this finding.

In summary, this study clearly demonstrates a relationship between LAMA3A expression and KLF4. The MCF10A cells which express LAMA3A express KLF4 and have high levels of KLF4 binding activity while all the breast cancer cell lines tested lacked KLF4 expression and activity. Laminin-5 in conjunction with many other pathways mediates the differentiation of mammary epithelial cells. Therefore, lack of KLF4 may attribute to the undifferentiated phenotype of breast cancer cells.

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REFERENCES
1. Stahl, S., Weitzman, S., and Jones, J. C. (1997) J. Cell Sci. 110, 55–63
2. Henning, K., Berndt, A., Katenkamp, D., and Kosmehl, H. (1999) Histopathology 34, 355–369
3. Martin, K. J., Kwan, C. P., Nagasaki, K., Zhang, X., O’Hare, M. J., Kaelin, C. M., Burgeson, R. E., Pardee, A. B., and Sager, R. (1998) Mol. Med. 4, 602–613
4. Virolle, T., Monthhourel, M. N., Djafari, Z., Ortonne, J. P., Meneguzzi, G., and Aberdam, D. (1998) J. Biol. Chem. 273, 17318–17325
5. Garrett-Sinha, I. A., Eberspaehcher, H., Seldin, M. F., and de Crombrugghe, B. (1999) J. Biol. Chem. 271, 31384–31390
6. Shields, J. M., Christy, R. J., and Yang, V. W. (1996) J. Biol. Chem. 271, 20009–20017
7. Jenkins, T. D., Opitez, O. G., Okano, J., and Rustgi, A. K. (1998) J. Biol. Chem. 273, 10747–10754
8. Yet, S. F., McNAMulty, M. M., Felts, S. C., Yen, H. W., Yohizumi, M., Hsieh, C. M., Layne, M. D., Chin, M. T., Wang, H., Perrella, M. A., Jain, M. K., and Lee, M. B. (1998) J. Biol. Chem. 273, 10296–10311
9. Tewari, R., Gillemsens, N., Wijgerde, M., Nuez, B., von Linden, M., Grosveld, F., and Philpsein, S. (1998) EMBO J. 17, 2334–2341
10. Anderson, K. P., Kern, C. B., Crable, S. C., and Lingrel, J. B. (1995) Mol. Cell. Biol. 15, 5957–5965
11. Matsumoto, N., Laub, F., Aldabe, R., Zhang, W., Ramirez, F., Yoshida, T., and Terada, M. (1998) J. Biol. Chem. 273, 28229–28237
12. Shi, H., Zhang, Z., Wang, X., Liu, S., and Teng, C. T. (1999) Nucleic Acids Res. 27, 4807–4815
13. Sogawa, K., Imataka, H., Yamasaki, Y., Kusume, H., Abe, H., and Fuji-Kuriyama, Y. (1993) Nucleic Acids Res. 21, 1527–1532
14. Crossley, M., Whitehall, E., Perkins, A., Williams, G., Fujii-Kuriyama, Y., and Orkin, S. H. (1996) Mol. Cell. Biol. 16, 1695–1705
15. Zhang, W., Shields, J. M., Sugawara, K., Fuji-Kuriyama, Y., and Yang, V. W. (1998) J. Biol. Chem. 273, 17917–17925
16. Miller, K. A., Chung, J., Lo, D., Jones, J. C., Thimmappaya, B., and Weitzman, S. A. (2000) J. Biol. Chem. 275, 8176–8182
17. Shields, J. M., and Yang, V. W. (1998) Nucleic Acids Res. 26, 796–802
18. Shie, J. L., Chen, Z. Y., Fu, M., Pestell, R. G., and Tseng, C. C. (2000) Nucleic Acids Res. 28, 2569–2576
19. Ferrigno, O., Virolle, T., Galliano, M. F., Chauvin, N., Ortonne, J. P., Meneguzzi, G., and Aberdam, D. (1997) J. Biol. Chem. 272, 20502–20507
20. Pulkkinen, L., Cserhalmi-Friedman, P. B., Tang, M., Ryan, M. C., Utito, J., and Christiano, A. M. (1998) Lab. Invest. 78, 1067–1076
21. Quandt, K., Frecch, K., Karras, H., Wingender, E., and Werner, T. (1995) Nucleic Acids Res. 23, 4878–4884
22. Virolle, T., Djafari, Z., Ortonne, J., and Aberdam, D. (2000) EMBO Rep. 1, 328–333
23. Brembeck, F. H., and Rustgi, A. K. (2000) J. Biol. Chem. 275, 28230–28239
24. Shie, J. L., Chen, Z. Y., O’Brien, M. J., Pestell, R. G., Lee, M. E., and Tseng, C. C. (2000) Am. J. Physiol. Gastrointest. Liver Physiol. 278, G806–814
25. Ton-That, H., Kaestner, K. H., Shields, J. M., Mahatankoon, C. S., and Yang, V. W. (1997) FEBS Lett. 419, 239–243
26. Dang, D. T., Bachman, K. E., Mahatan, C. S., Dang, L. H., Giardelli, F. M., and Yang, V. W. (2000) FEBS Lett. 476, 203–207
27. Mahatan, C. S., Kaestner, K. H., Geiman, D. E., and Yang, V. W. (1999) Nucleic Acids Res. 27, 4562–4569