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ORIGINAL ARTICLE

Ultraviolet B Downregulated Aquaporin 1 Expression via the MEK/ERK pathway in the Dermal Fibroblasts

Won-Oh Kim, Sung-Ae Kim, Yun-A Jung, Sung-Il Suh[1], Young-Wook Ryoo

Departments of Dermatology and [1]Microbiology, Institute for Medical Science, School of Medicine, Keimyung University, Daegu, Korea

Background: Aquaporin 1 (AQP1) is a transmembrane channel protein that allows rapid transposition of water and gases, in recent discoveries of AQP1 function involve cell proliferation, differentiation, wound healing, inflammation and infection in different cell types, suggesting that AQP1 plays key roles in diverse biologic process. Until now, less is known about the function of AQP1 on ultraviolet radiation induced photoaged skin. **Objective:** In this study we set out to examine whether AQP1 expression may be influenced by repeated irradiation of ultraviolet B (UVB) in cultured dermal fibroblasts. **Methods:** To elucidate the function of AQP1 in skin photoaging, human dermal fibroblasts (HS68) were irradiated by a series of 4 sub-cytotoxic doses of UVB which are known as UV-induced cell premature senescence model. Reverse transcription polymerase chain reaction and Western blotting were conducted to detect AQP1 expression from different groups. Then, cells were transfected with AQP1-targeting small interfering RNA. The activities of signaling proteins upon UVB irradiation were investigated to determine which pathways are involved in AQP1 expression. **Results:** AQP1 expression was increased by 100 mJ/cm^2 of UVB irradiation, but decreased by 200 mJ/cm^2. Depletion of the AQP1 increased the apoptotic sensitivity of cells to UVB, as judged by upregulation of the p53, p21, poly (adenosine diphosphate [ADP]-ribose) polymerase and Bax together with the increased Bax/Bcl2 ratio. UVB induced downregulation of AQP1 was significantly attenuated by pretreatment with the MEK/ERK inhibitor (PD98059). **Conclusion:** We concluded that AQP1 expression was down-regulated by repeated exposure of UVB via MEK/ERK activation pathways. The AQP1 reduction by UVB lead to changes of physiological functions in dermal fibroblasts, which might be associated with the occurrence and development of UVB induced photoaging. **(Ann Dermatol 32(3) 213～222, 2020)**

-Keywords-
Aquaporin 1, Human dermal fibroblast, MEK/ERK pathway, Ultraviolet B

INTRODUCTION

Aquaporins (AQPs) are a family of hydrophobic, integral transmembrane proteins that facilitate transport of water, some gases, and small solutes[1]. At least, thirteen AQPs have been identified and are expressed in various epithelial and endothelial cells in mammalian[1]. AQP0, AQP1, AQP2, AQP4, AQP5, and AQP8 are water transporters, whereas AQP3, AQP7, AQP9, and AQP10 transport glycerol and other small solutes in addition to water and are therefore known as aquaglyceroproteins[2].

Recently, extensive data demonstrate that the functions of AQPs is not only a water transporter but also a biologic mediator in many different cell types that were originally thought not to carry out fluid transport[3]. In addition, growing evidence suggests that those proteins are involved in cell proliferation, differentiation, apoptosis and tumor progression[4,5]. Under stressful condition, such as hypertonic stress, the expression of AQP1 was up-regulated to survive in the fibroblast[6,7] and inhibiting the expression of AQP1

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Corresponding author: Young-Wook Ryoo, Department of Dermatology, School of Medicine, Keimyung University, 1095 Dalgubeol-daero, Dalseo-gu, Daegu 42601, Korea. Tel: 82-53-258-4561, Fax: 82-53-258-4566, E-mail: ryoo111@dsmc.or.kr
ORCID: https://orcid.org/0000-0002-2477-6263

leads to apoptosis human lens epithelial cells[8]. In the dermatologic field, the AQP1 and AQP3 are expressed in dermis and epidermis of the skin, respectively[2], but few researches has been done about the relationship between AQ1 and ultraviolet (UV), which are main external stressful factor to the skin.

UV radiation is a major environmental threat to the skin[9,10]. Ultraviolet B (UVB) radiation penetrates the epidermis reaches the upper dermis, can directly damage DNA and induce apoptosis[11]. Furthermore, chroninc exposure of UVB irradiation can cause photoaging[10], photoimmunosuppression, and photocarcinogenesis in the skin, and many attempts are being made to prevent those harmful effects of UV radiation[12]. In the previous reports, the relationship between AQP3 and UV has been demonstrated in epidermis and keratinocyte in culture[13]. The UV radiation downregulates AQP3 in keratinocytes[14] and, Xie et al.[15] reported that the protective role of AQP3 in UVA-induced apoptosis via Bcl2 up-regulatory mechanism, but the role of AQP1 in dermal fibroblast under UV radiation has not been studied. Long-term exposure of skin to solar radiation causes premature skin aging, photoaging and the important features of photoaged skin are severe wrinkles and dermal atrophy, which mainly due to dysfunction of dermal fibroblasts by life long accumulative effects of UV exposure[16]. Therefore, we focused on whether the AQP1 play a role in fibroblasts when developing photoaging of skin which are the main cells responsible for remodeling of extracellular matrix in the dermis. Hence, an examination of the repetitive effects of UV exposure to fibroblast is more likely to yield clues to the early alterations that lead to photoaged skin than a single exposure[9]. Borlon et al.[17] had been carried out to elucidate the cumulative effects of UVB in the human dermal fibroblast using the model of repeated exposure to a sub-cytotoxic dose of UVB (2.5 kJ/m^2) can induce premature senescence.

We hypothesized that AQP1-apoptosis system as a putative component of the protective machinery against repetitive UVB-induced fibroblast damages and in the current study, we used the model of premature senescence by a series of 4 sub-cytotoxic UVB exposures of dermal fibroblasts which are already been studied[9]. To verify whether AQP1 protects fibroblasts under UVB-induced apoptosis, we assessed expression of p53, p21, poly (adenosine diphosphate [ADP]-ribose) polymerase (PARP), Bax, and Bcl2 following small interfering RNA (siRNA)-mediated depletion of AQP1. Our novel findings suggested that the water transporting protein AQP1 participate in protective mechanism against repeated irradiation of UVB induced photodamages in dermal fibroblasts.

MATERIALS AND METHODS

This study was reviewed and declared exempt from Institutional Review Board approval.

Cell culture

HS68 human dermal fibroblasts (CRL-1635; ATCC, Manassas, VA, USA) were maintained in Dulbecco's Modified Eagle's Medium (Welgene, Gyeongsan, Korea) supplemented with 10% fetal bovine serum (Welgene) and penicillin-streptomycin solution (Welgene). Cells were grown for several weeks in cell culture dishes in a humidified atmosphere containing 5% CO_2 and 95% at 37°C. Confluent monolayers were detached by treatment with 1× trypsin-EDTA solution (Welgene) and re-plated at a dilution of 1:2. Cells of passage 6 to 10 were used for the following experiments.

Chemicals and antibodies

An anti-AQP1 antibody was obtained from Abcam (Cambridge, UK). Antibodies against p53, PARP, Bax, Bcl2, p-p38, p-38, p-ERK, and T-ERK were obtained from Cell Signaling Technology (Danvers, MA, USA). Anti-p21 and anti-GAPDH antibodies were obtained Santa Cruz Biotechnology (Santa Cruz, CA, USA). SB203580 and PD98059 were obtained from TOCRIS (Bristol, UK).

UVB irradiation

At 48 hours prior to the first UVB irradiation, HS68 cells at 55% to 60% of confluency were sub-cultured at a density of 1×10^5 cells/cm^2 in Dulbecco's Modified Eagle's Medium containing 1% fetal bovine serum. Cells were washed twice with phosphate-buffered saline (PBS; 10 mM NaCl, pH 7.4) and irradiated with UVB in a thin layer of PBS using a Westinghouse FS40 sunlamp (National Biological Corp., Twinsburg, OH, USA). UVB radiation peaked at 310 to 315 nm and the lamp was placed 30 cm above the cells. The emitted radiation was checked using a UV radiometer equipped with a UVB sensor (Waldmann Lichttechnik, Villingen-Schwenningen, Germany). Cells were irradiated twice (12 hours interval) per day for 2 days. Control cells were cultured under the same conditions but were not irradiated.

Cell count and proliferation assay

The effect of UVB on cell viability and proliferation assay were determined using WST-8 dye (Cell Counting Kit-8 [CCK-8]; Dojindo molecular technologies, Inc., Rockville, MD, USA) according to manufacturer's instructions. Briefly, 4×10^3 cells/well were seeded in a 96-well flat-bottomed plate. After overnight incuba-tion, the cells were treated with UVB at increasing doses and then cultured in the

presence of 10% FBS in DMEM for another 24 hours. After 10 μl CCK-8 solution was add to each well, cells were incubated at 37°C for 2 hours and the absorbance was finally determined at 450 nm using micrpplate Reader (Thermo Electron Corp., Waltham, MA, USA). The reduction in viability of in UVB-treated fibroblasts was expressed as a percentage compared to non-treated cells and control cells were considered to be 100% viable.

RT-PCR analysis

Total RNA was extracted in triplicate from confluent cells in 75 cm^2 cell culture flasks using an RNeasy kit (Qiagen, Courtaboeuf, France). Reverse transcription polymerase chain reaction (RT-PCR) was performed using a SuperScript One-Step RT-PCR System and Platinum Taq (Invitrogen, Carlsbad, CA, USA). Each reaction contained 100 ng (1 μl) of total RNA in a total volume of 50 μl. Reverse transcription was performed at 50°C for 30 minutes, followed by 35 PCR cycles with an annealing temperature of 60°C. Amplification products were detected by electrophoresing 10 μl of the reaction product in a 2% agarose gel following by ethidium bromide staining. The identities of the amplification products were confirmed by their size and by analysis of their digestion profiles upon treatment with specific restriction enzymes. The PCR primer sequences and the expected lengths of the amplicons were as follows: AQP1 (188 bp), sense 5′-AGGCTACAAAGCAGAGATCGAC-3′ and antisense 5′-CACCCTCTAAATGGCTTCATTC-3′; and β-actin (209 bp), sense 5′-GCCGTCTTCCCCTCCATCGTG-3′ and antisense 5′-GGAGCCACACGCAGCTCATTGTAGA-3′.

siRNA transfection

Human AQP1-targeting siRNA (siAQP1, Cat# sc-29711) and control siRNA (siCon, Cat# sc-37007) were purchased from Santa Cruz Biotechnology. Cells were transfected with siRNAs in Opti-MEM (GIBCO, Grand Island, NY, USA) using Lipofectamine 2000 (Invitrogen) for 5 hours according to the manufacturer's recommendations and incubated in a CO_2 incubator for 24 hours at 37°C.

Western blot analysis

Cells were harvested after UVB treatment for 24 and 48 hours, washed thrice with PBS and resuspended in ice-cold buffer containing 50 mM Tris, 150 mM NaCl, 1 mM ethylenediaminetetraacetic acid, 1% Triton X-100, 0.5% sodium deoxycholate, and protease/phosphatase inhibitors (GenDEPOT, Barker, TX, USA). Cell lysates were centrifuged at 12,000 g for 10 minutes, and the supernatants were collected. Samples were separated on 6.5% to 12% sodium dodecyl sulfate-polyacrylamide gels and transferred to polyvinylidene difluoride membranes (Millipore, Billerica, MA, USA). Membranes were blocked with 5% skimmed milk prepared in Tris-buffered saline containing 0.1% Tween-20 and incubated with an anti-AQP1 antibody diluted 1:500 (Abcam) overnight at 4°C. After that, membranes were washed and incubated with horseradish peroxidase-conjugated mouse IgG diluted 1:2,500 (GeneTex, Irvine, CA, USA) at room temperature for 1 hour. Complexes were visualized by enhanced chemiluminescence using ECL western Detection Reagents (Amersham Pharmacia Biotech, Piscataway, NJ, USA). Signals were detected using a chemiluminescence detection system (Vilber, Collégien, France).

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics ver. 23.0 (IBM Corp., Armonk, NY, USA). Multiple groups were compared using an analysis of variance followed by Duncan's *post hoc* test. Data are expressed as the mean ± standard error of the mean (SEM). $p < 0.05$ was considered statistically significant.

RESULTS

UVB irradiation affects AQP1 expression

Hs68 cells were irradiated with 0, 50, 100, 200, and 300 mJ/cm^2 of UVB and the AQP1 expressions were detected by RT-PCR and Western blotting. The AQP1 expressions were increased by irradiation with low doses (50, 100 mJ/cm^2) of UVB, but decreased by irradiation with high doses (200, 300 mJ/cm^2) of UVB (Fig. 1). These data suggest that AQP1 expression might take part in regulating cellular homeostasis under UVB stress and provides evidence to support possible protective effect of AQP1 in UVB induced skin alterations.

UVB irradiation inhibited cell viability and proliferation

To find out the proper dose of UVB irradiation which may lead to apoptosis, we test the cytotoxic effect of UVB at 0, 100, 200 mJ/cm^2 irradiation doses. As expected, cell number declined significantly in a dose-dependent manner. The cell viability was further examined using CCK-8 assay (Fig. 2). Therefore, the dose 200 mJ/cm^2 was defined as pro-apoptosis and the sub-cytotoxic dose, 100 mJ/cm^2 was used throughout this experiment.

UVB irradiation affects AQP1, p53, p21, and PARP expression

To determine the relationship between AQP1 expression and UVB-induced apoptosis of fibroblasts, Hs68 cells were irradiated with 0, 100, and 200 mJ/cm^2 of UVB and the expressions of AQP1, p53, p21, and PARP were assessed by Western blotting. Consistent with the previous findings,

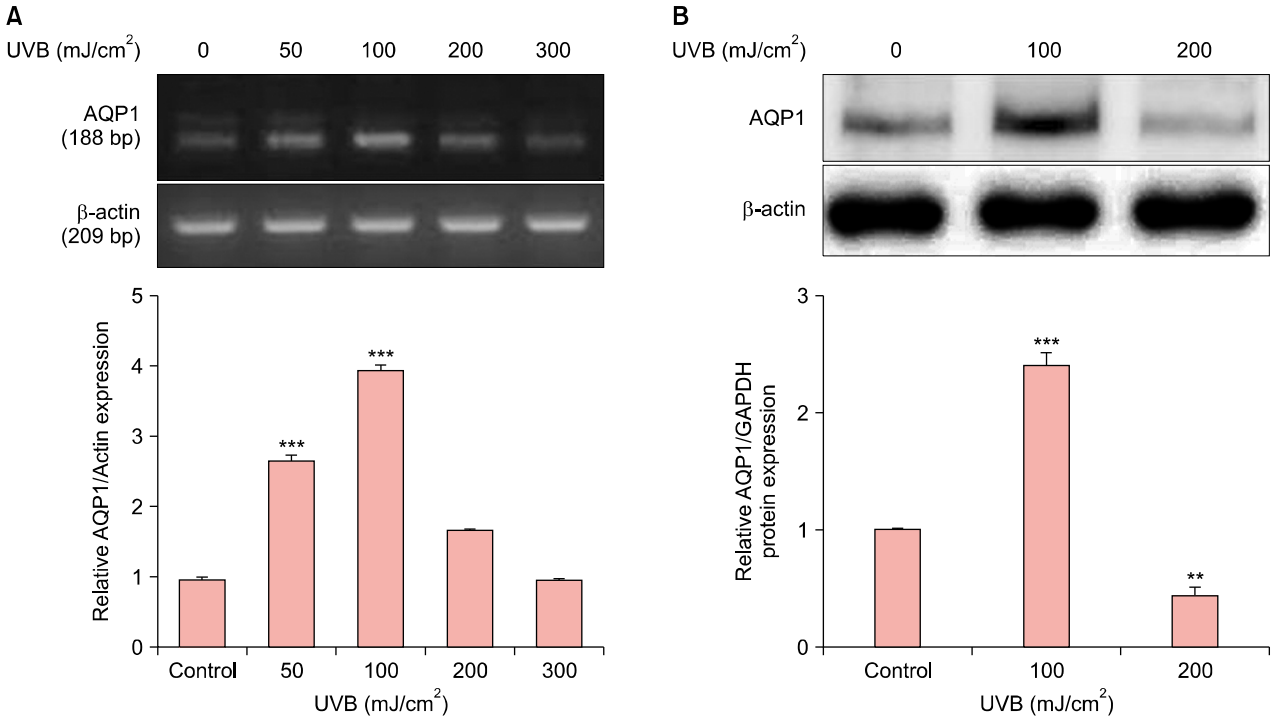

Fig. 1. Ultraviolet B (UVB) irradiation changes aquaporin 1 (AQP1) expression. (A) HS68 cells were irradiated with 0, 50, 100, 200, or 300 mJ/cm^2 UVB and collected 24 hours later. Reverse transcription polymerase chain reaction (RT-PCR) was performed to detect the mRNA expression of AQP1. (B) Cells were irradiated with 0, 100, or 200 mJ/cm^2 UVB and collected 24 hours later. An equal amount (30 μg) of protein was analyzed by Western blotting with a polyclonal anti-AQP1 antibody. β-Actin was used as a loading control. Values are presented as mean±standard error of the mean of three independent experiments. $^{**}p<0.01$, $^{***}p<0.001$ vs. control.

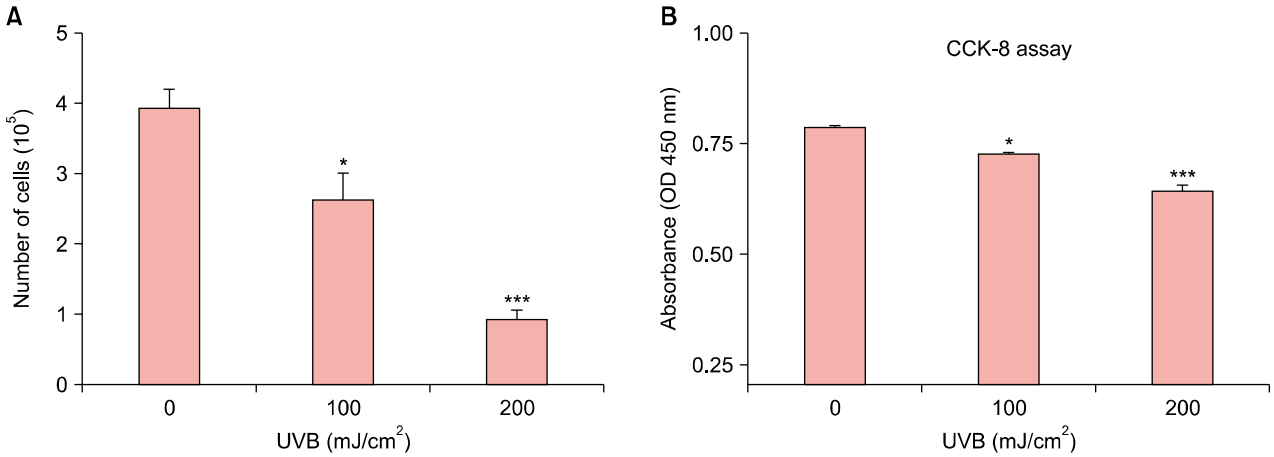

Fig. 2. Ultraviolet B (UVB) irradiation induces decrease of cell viability in a dose-dependent manner. (A) Viability of cells was determined by cell count. (B) And cell proliferation and cytotoxicity assay were determined by the Cell Counting Kit-8 (CCK-8) assay. Dose-dependent effect of UVB irradiation on fibroblasts cell viability and proliferation were observed. Values are presented as mean±standard error of the mean of three independent experiments. OD: optical density. $^{*}p<0.05$, $^{***}p<0.001$ compared with 0 mJ/cm^2 of UVB).

we found that low doses of UVA irradiation (100 mJ/cm^2) up-regulated AQP1 expression (Fig. 1B), but did not induce apoptotic changes in dermal fibroblasts. However, high doses of UVB irradiation (200 mJ/cm^2) down-regulated AQP1 and the expressions of p53, p21, and cleaved PARP were significantly increased (Fig. 3).

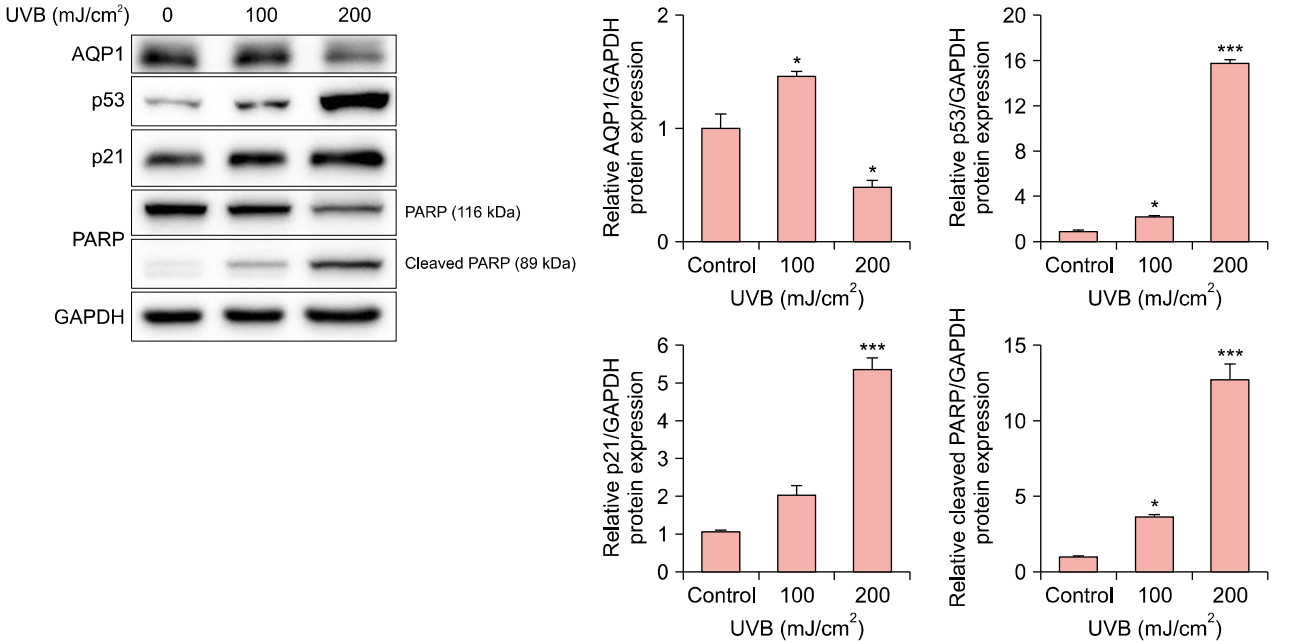

Fig. 3. Ultraviolet B (UVB) irradiation affects the expression of aquaporin 1 (AQP1), p53, p21, and PARP. HS68 cells were irradiated with 0, 100, or 200 mJ/cm^2 UVB and collected 24 hours later. An equal amount of protein was analyzed by Western blotting. Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as a loading control. Values are presented as mean±standard error of the mean of three independent experiments. *$p<0.05$, ***$p<0.001$ vs. control.

Transfection of siAQP1 reduces AQP1 expression

To investigate whether AQP1 take part in biologic process under UVB-induced stress, we generated AQP1-silenced HS68 cell. The AQP1 expression was significantly decreased in siAQP1-transfected cells than siCon-transfected and control cells. The AQP1 expressions were comparable in control and siCon-transfected cells. These results demonstrate that transfection of siAQP1 clearly reduces AQP1 expression in dermal fibroblasts (Fig. 4).

AQP1 protects against UVB-induced apoptosis of dermal fibroblasts

To investigate the potential role of AQP1 in protecting dermal fibroblasts against UVB-induced apoptosis, we assessed expression of p53, p21, PARP, Bax, and Bcl2, as well as the Bax/Bcl2 ratio, in cells which were depleted of AQP1. Expression of the pro-apoptotic markers p53, p21, cleaved PARP, and Bax was higher in siAQP1-transfected cells than in siCon-transfected cells and control following irradiation with 200 mJ/cm^2 of UVB. However, expression of the anti-apoptotic marker Bcl2 was significantly decreased in HS68 cells after irradiation 200 mJ/cm^2 UVB. Moreover, the Bax/Bcl2 ratio was significantly higher in siAQP1-transfected cells (Fig. 5). These findings demonstrate that depletion of AQP1 sensitizes HS68 cells to UVB-induced apoptosis.

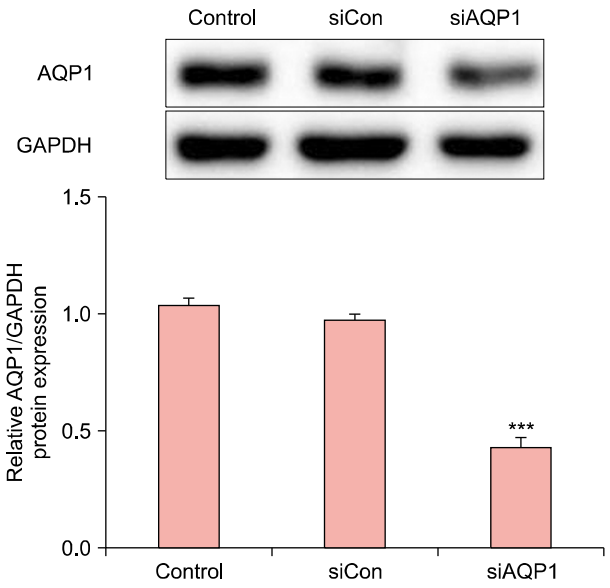

Fig. 4. Transfection of siAQP1 reduces AQP1 expression. HS68 cells were transfected with siCon or siAQP1. An equal amount of protein was analyzed by Western blotting. GAPDH was used as a loading control. Values are presented as mean±standard error of the mean of three independent experiments. AQP1: aquaporin 1, siAQP1: aquaporin 1-targeting small interfering RNA, siCon: control small interfering RNA, GAPDH: glyceraldehyde 3-phosphate dehydrogenase. ***$p<0.001$ vs. siCon.

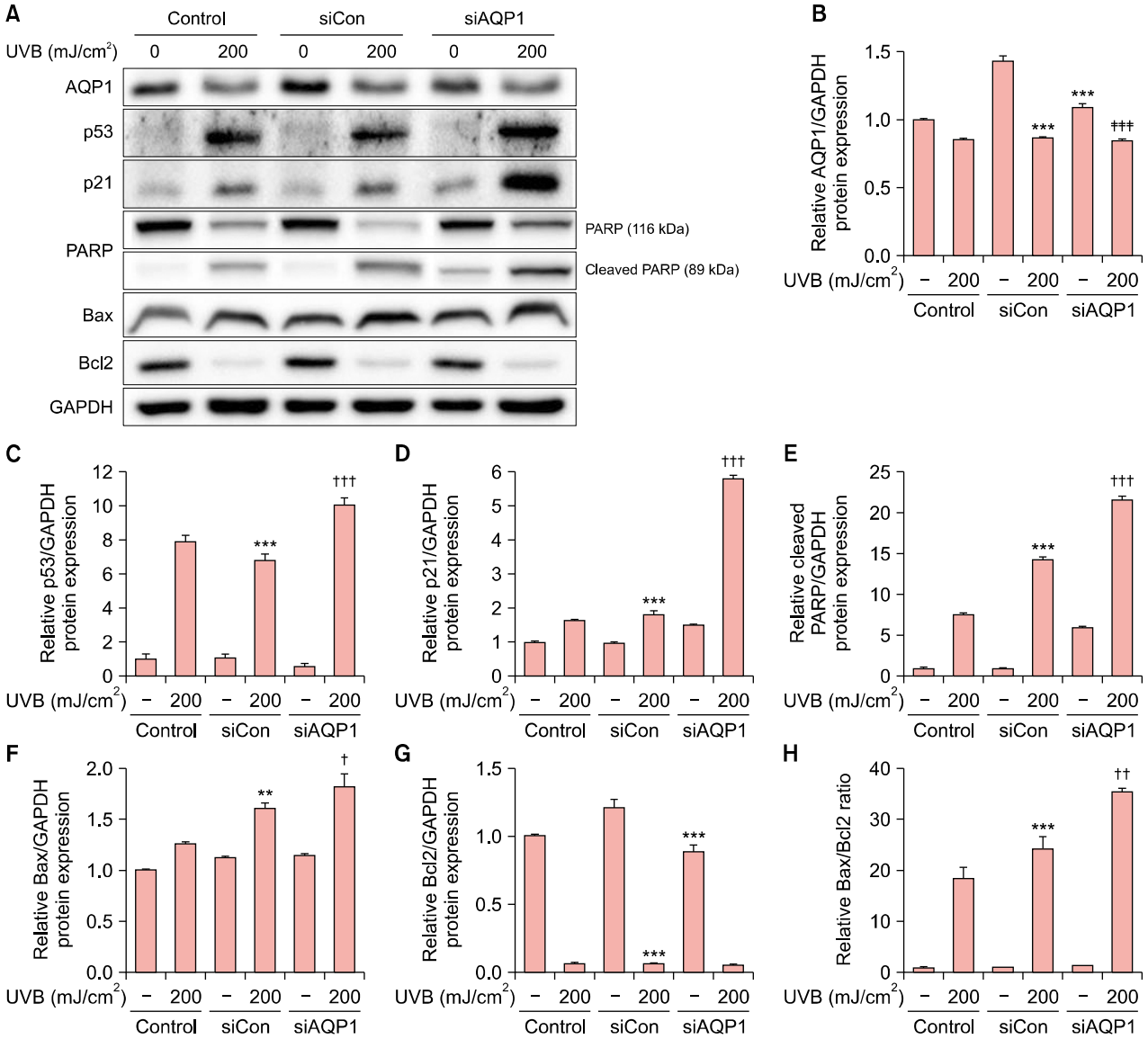

Fig. 5. AQP1 protects against UVB-induced apoptosis. (A) Control, siCon-transfected, and siAQP1-transfected HS68 cells were irradiated with 0 or 200 mJ/cm^2 UVB and collected 24 hours later. Expression of AQP1, p53, p21, PARP, Bax, and Bcl2 was analyzed by Western blotting. (B~G) The band densities were determined. GAPDH was used as a loading control. Values are presented as mean±standard error of the mean of three independent experiments. $^{**}p<0.01$, $^{***}p<0.001$ vs. siCon UVB 0 mJ/cm^2; $^{\dagger}p<0.05$, $^{\dagger\dagger\dagger}p<0.001$ vs. siCon UVB 200 mJ/cm^2; and $^{\ddagger\ddagger\ddagger}p<0.001$ vs. siAQP1 UVB 0 mJ/cm^2. (H) The Bax/Bcl2 ratio was evaluated. UVB: ultraviolet B, AQP1: aquaporin 1, siAQP1: aquaporin 1-targeting small interfering RNA, siCon: control small interfering RNA, GAPDH: glyceraldehyde 3-phosphate dehydrogenase. $^{***}p<0.001$ vs. siCon, $^{\dagger\dagger}p<0.01$ vs. siCon UVB 200 mJ/cm^2.

The MEK/ERK and p38 signaling pathways are activated by UVB in dermal fibroblasts

Next, we examined the consequence of UVB-induced AQP1 down regulation. We tested two well known downstream kinase casdade poteins, p38 and ERK which are related UV radiation. The phosphorylated forms of p38 and ERK were detected in HS68 cells following irradiation with 200 mJ/cm^2 UVB and those phosphorylations were significantly inhibited by pretreatment with SB203580 (p38 inhibitor) and PD98059 (MEK/ERK inhibitor), respectively (Fig. 6).

Inhibition of MEK/ERK activation is involved in UV-induced down-regulation of AQP1

Our work above has clearly demonstrated that UVB induced down regulation of AQP1; however, the mechanisms have not been studied. To answer that question, we used MEK/ERK and p38 inhibitors. As showing in Fig. 6, UVB

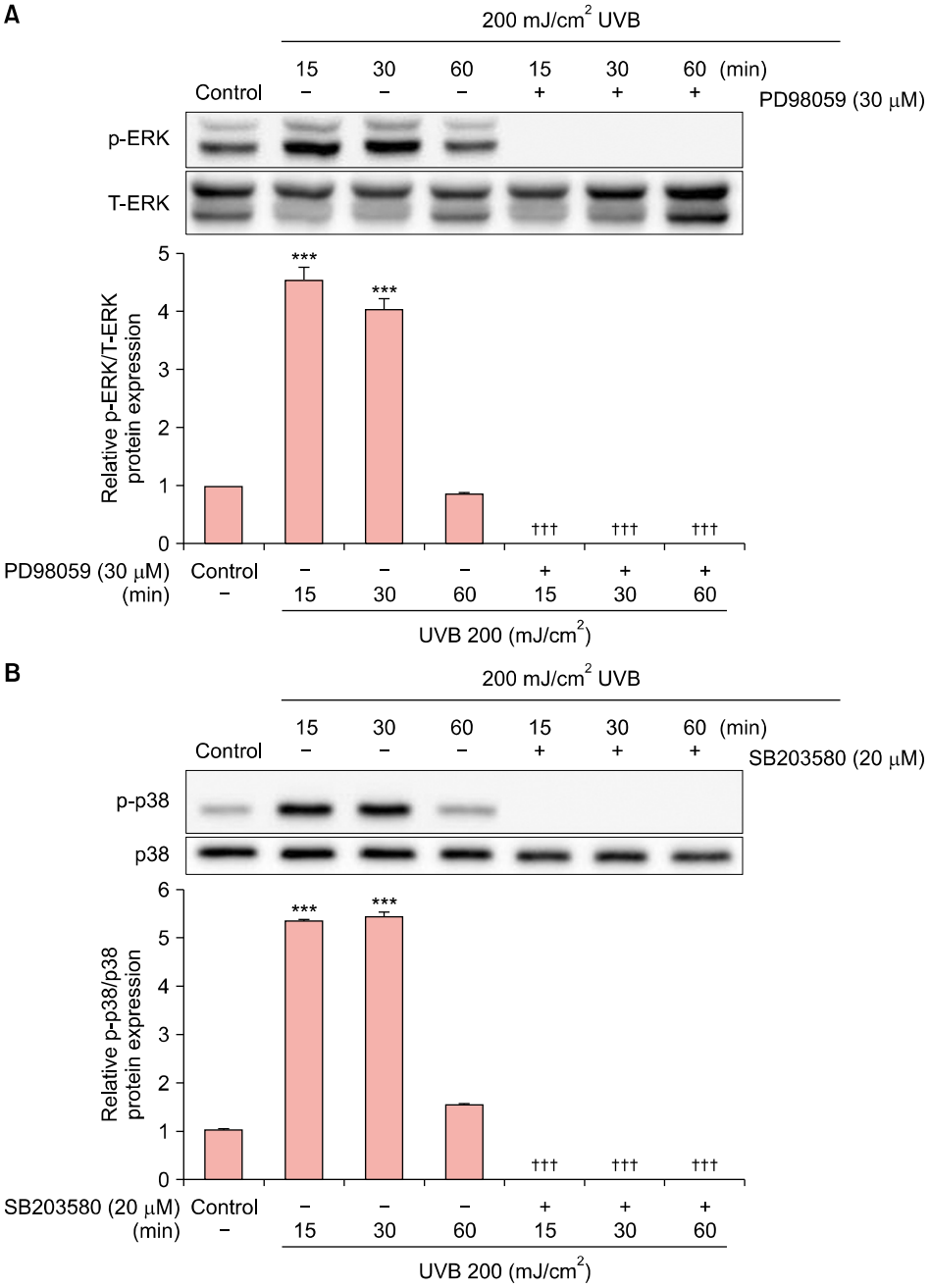

Fig. 6. The MEK/ERK and p38 signaling pathways are involved in ultraviolet B (UVB)-induced apoptosis. HS68 cells were pretreated with and without a MEK/ERK inhibitor (PD98059) (A) or a p38 inhibitor (SB 203580) (B) and collected 15~60 minutes after irradiation with 200 mJ/cm^2 UVB. An equal amount of protein was analyzed by Western blotting. Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as a loading control. Values are presented as mean±standard error of the mean of three independent experiments. ***$p<0.001$ vs. control; †††$p<0.001$ vs. UVB 200 mJ/cm^2 15 minutes.

irradiation-induced downregulation of AQP1 was blocked by pretreatment with the PD98059, MEK/ERK inhibitor (Fig. 7). These results demonstrate that activation of the MEK/ERK pathway is involved in UVB-induced downregulation of AQP1.

DISCUSSION

UVB are known to interact with cellular chromophores and photosensitizers, resulting in the generation of reactive oxygen species, induction of potentially mutagenic DNA damage, and activation of signaling pathways leading to changes in the expression of genes related to growth, differentiation, senescence and connective tissue degradation[10]. Life long accumulation of UV exposure is the main cause of extrinsic skin aging[18,19], which the feature is disorganization of extracellular matrix of dermis resulted in severe coarse wrinkles and skin atrophies relative to intrinsic aged skin[11]. Therefore, many studies have been conducted on the effects of UV on dermal fibroblasts. Recently, increasing attention has been paid to the role of AQP in the pathogenesis of UB induced skin damages[13,19].

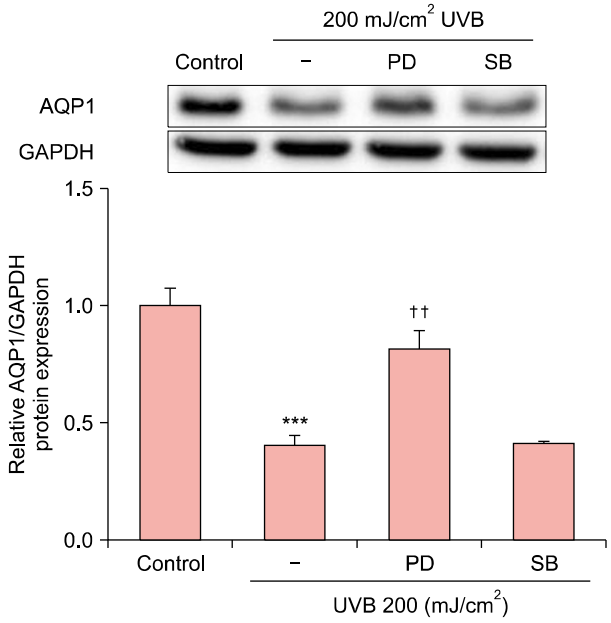

Fig. 7. Treatment with a MEK/ERK inhibitor attenuates ultraviolet B (UVB)-induced downregulation of aquaporin 1 (AQP1). HS68 cells were pretreated with a MEK/ERK inhibitor (PD98059 [PD]) or a p38 inhibitor (SB203580 [SB]) and collected 24 hours after irradiation with 200 mJ/cm^2 UVB. An equal amount of protein was analyzed by Western blotting. Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as a loading control. Values are presented as mean±standard error of the mean of three independent experiments. ***$p<0.001$ vs. control; $^{\dagger\dagger}p<0.01$ vs. Only UVB 200 mJ/cm^2.

AQPs are mainly expressed in endothelial cells, fibroblast, nerve cells and glomerular cells, and primarily act as a water-selective pore and facilitates osmotically driven water transport across the plasma membrane[1]. Recently, AQPs also expressed in cell types that were originally thought not to carry out fluid transport[5], and they played a critical role in cell migration, proliferation, and differentiation, apoptosis and tumorigenesisby altering the cell cycle progression but the precise mechanisms are still unknown[3,4]. Zheng et al.[8] reported that the AQP1 down regulation associated with inhibiting cell viability and inducing apoptosis of human lens epithelial cell. This led us to speculate that AQP1 may participate in the early cellular response to stressful condition such as UVB radiation. This study focuses on the relationship between the expression of AQP1 and UVB induced damages in dermal fibroblast.

After single dose of UVB, we did not found any significant changes the expression of AQP1(data notshown). As a result of using the method for photoaging model of Zeng et al.[9], the 4 repeated UVB radiation method, the AQP1 expressions were changed, so we thought that the AQP1 might be involved in UVB induced skin photoaging. We found that the AQP1 expression was increased at 100 mJ/cm^2 of UVB. This up-regulation of AQP1 is thought to be one of the self protection machanisms against apoptotc damage of dermal fibroblasts under a low dose of UVB.

Our findings suggest that this is a new function of AQP1 other than the role of water passage in fibroblast. Those our results are consistent with recent finding that up-regulation AQPs are involved in many physiological and pathological functions by altering the expression of key proteins for cell cycle progression[4]. For example, AQP4 is up-regulated within the glial scar in response to brain injury *in vivo*[5,14,18]. AQP3 is upregulated in dehydration condition in the kidneys[20], AQP1 upregulated in hypoxic condition in the lungs[21], and a low dose of UVA radiation upregulates AQP3 in cultured keratinocytes[22,23]. However, the expression of AQP1 was decreased at repepated exposure of 200 mJ/cm^2 of UVB. As expected, high doses of UVB radiation induced phosphorylation of apoptotic markers such as p53, p21, and PARP. Those our results are consistent with recent finding that the accumulated UVB stress will cause premature aging or cell death by activation of proliferation and survival signaling pathways[16,17]. The other question that remains unanswered is wheather AQP1 is directly involved in UVB induced dermal fibroblast apoptotic chamges, thus we used the siRNA tech to knockdown the AQP1. We found that the expression of p53, p21, cleaved PARP, Bax, and Bax/Bcl2 ratio were higher in siAQP1-transfected cells than control at 200 mJ/cm^2 UVB. These results clearly demonstrate that that AQP1 involved in UVB-induced apoptotic changes in derma fibroblasts. Increasing experimental data suggest that UV light is mediated by signal transduction mostly dependent on mitogen activated protein kinases (MAPKs); particularly the p38, Jun amino-terminal kinase (JNK)/stress-activated protein kinases (SAPK) and extracellular signal-regulated kinases (ERK)[24-26]. Therefore, we investigated expression of those signaling molecules to elucidate which signal pathways are involved in UVB-induced downregulation of AQP1. Among them, we found the phosphorylation of ERK and p38 were increased Irradiation with 200 mJ/cm^2 of UVB. Therefore, we focused on the role of ERK and p38 phosphorylation in UVB-induced downregulation of AQP1. The pretreatment with PD98059 (MEK/ERK inhibitor) group showed that significantly attenuated UVB-induced downregulation of AQP1. Collectively, it is highly likely that PD98059 (MEK/ERK inhibitor) inhibit UVB-induced AQP1 downregulation.

We conclude that attenuation of UVB-induced apoptosis by AQP1 is a putative component of the regulatory network that protects the skin against UVB-induced damage. Similarly, Jiang et al.[27] reported that the MEK/ERK pathway

mediates UVB-induced downregulation of AQP1 in human retinal pigment epithelial cells (ARPE-19). Our data strongly indicate that the protective role of AQP1 is against UVB-induced cellular damage. However, it remains uncertain whether this effect is independent of water transport by AQP1, so further studies are required to investigate this issue and the more precise mechanisms and roles of AQP1 in photoaging must be explored further.

In this study, we demonstrated for the first time, the patterns of AQP1 expressions and its protective role and potential regulatory mechanisms in dermal fibroblast in response to repetitive UVB exposure. Thus, AQP1 is likely to be an one of the important proteins in the field of photoaging research, in the future.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

ORCID

Won-Oh Kim, https://orcid.org/0000-0001-6826-6444
Sung-Ae Kim, https://orcid.org/0000-0002-6040-6630
Yun-A Jung, https://orcid.org/0000-0001-6095-6264
Sung-Il Suh, https://orcid.org/0000-0003-2078-292X
Young-Wook Ryoo, https://orcid.org/0000-0002-2477-6263

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