Sunlight Exposure–Mediated DNA Damage in Young Adults

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Abstract

Background: Previous experimental studies showed that single ultraviolet B (UVB) light irradiation increased levels of 8-hydroxy-2′-deoxyguanosine (8-OHdG), a well-established biomarker of carcinogenesis and oxidative DNA damage, in epithelial cells in animals and humans. We conducted for the first time an epidemiologic study to investigate the correlations among levels of oxidative DNA damage, skin pigmentation, and sunlight exposure in human daily life.

Methods: Digitalized skin pigmentation levels and creatinine-adjusted urinary 8-OHdG levels were examined in 127 healthy young adults aged 20 to 24 years and in hairless mice with normal pigmented skin (HL-mice; $n = 20$) and hyperpigmented skin (HL-HPS-mice; $n = 20$). Data obtained by a questionnaire were also analyzed for the 127 subjects.

Results: Binary logistic regression analysis showed that increased sunlight intensity, but not sunlight-exposed time or sunlight-exposed skin area, was correlated with elevation in creatinine-adjusted urinary 8-OHdG levels. In contrast, increased skin pigmentation level, but not the use of sunscreen, was correlated with reduction in urinary 8-OHdG level in humans. UVB irradiation corresponding to several minutes of sunlight exposure significantly increased urinary 8-OHdG levels in HL-mice but not in HL-HPS-mice.

Conclusions: We showed that increase in intensity of sunlight in human daily life increased levels of DNA damage. We also showed a protective effect of skin pigmentation on sunlight exposure–mediated DNA damage.

Impact: We have provided more reliable evidence of routine sunlight exposure–mediated DNA damage in humans through the combination of epidemiologic and experimental studies. *Cancer Epidemiol Biomarkers Prev; 20(8); 1622–8. ©2011 AACR.*

Introduction

Epidemiologic studies have shown that exposure to sunlight is associated with the development of various cutaneous disorders including cancer (1, 2). Experimental studies have revealed that ultraviolet (UV) light is a major causal factor in sunlight-mediated cutaneous diseases including cancer (3). UV works as an oxidative stressor via promotion of free radical production (1, 2). Our previous study showed that UV-mediated oxidative stress directly enhanced oncogene product activity through its conformational change (4). UV-mediated production of free radicals also causes various types of DNA damage such as DNA single- and double-strand breaks, base modifications, and abasic sites (1, 2). Therefore, appropriate blocking of sunlight including UV is believed to be necessary for the promotion of health in humans.

8-Hydroxy-2′-deoxyguanosine (8-OHdG) is one of the predominant forms of free radical–induced oxidative lesions (1, 2, 5). 8-OHdG has been used as a well-established biomarker for the measurement of endogenous oxidative DNA damage (1, 2). Various carcinogenic substances, environmental pollutants, and lifestyle factors affect the levels of 8-OHdG (1, 2). Sunlight and UV irradiation have been also reported as risk factors for increased 8-OHdG levels in epidermal cell lines *in vitro* and in the skin of animals and humans *in vivo* (6–10). However, there has been no study reported in which the influence of sunlight exposure in human daily life on 8-OHdG levels was clarified.

Sensitivity of Caucasians to induction of skin disorders by sunlight and UV irradiation has been shown to be higher than that in Africans and Asians (11). These results suggest that skin pigmentation plays an important role in protection against sunlight and UV radiation. To our knowledge, however, there has been no study on the effect of skin pigmentation on DNA damage in human daily life.

In this study, we examined for the first time sunlight exposure–mediated oxidative DNA damage in human

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daily life by urinary 8-OHdG levels. We also investigated the correlation between oxidative DNA damage and digitalized skin pigmentation level by using a reflectance spectrophotometer in each subject (12–14). On the basis of our epidemiologic results, we experimentally examined the effect of ultraviolet B (UVB) light irradiation on urinary 8-OHdG levels in hairless mice (HL-mice). We also examined the effect of skin pigmentation on UV-mediated DNA damage by using HL-mice with hyper-pigmented skin (HL-HPS-mice; ref. 15). These dual investigations in humans and mice provided novel evidence of correlations among sunlight including UV, skin pigmentation, and DNA damage.

Methods

Subjects and questionnaires in the human study

A total of 127 healthy subjects (62 males and 65 females) aged 20 to 24 years participated in this study in Aichi Prefecture of Japan from the end of May to the beginning of June in 2009 and 2010 after giving informed consent. All subjects answered a questionnaire after being informed of topical outlines of the questionnaire including the rule of nines (16). Sunlight-exposure time (hours per day) was defined as the total number of hours during which the subjects go outdoors in the daytime on a sunny day. Ratio of sunlight-exposed skin area to the whole body in subjects who stayed outdoors for more than 5 minutes in the daytime on a sunny day was evaluated by the rule of nines (16). Average of sunlight intensity including UV intensity ($J/cm^2/d$) in subjects who stayed outdoors for more than 5 minutes in the daytime on a sunny day was calculated from published data for Nagoya City in Aichi Prefecture from the Japan Meteorological Agency. We also measure the intensity of ultraviolet A (UVA; mW/cm^2) and UVB ($\mu W/cm^2$) in sunlight by a microvolt ampmeter (UVR-3036/S; Topcon Corporation). A previous study showed that cutaneous 8-OHdG levels were maximally increased 24 to 48 hours after single UVB irradiation in humans, whereas there has been no report showing urinary 8-OHdG levels. Therefore, sunlight exposure time, sunlight-exposed skin area, and sunlight intensity were examined 1 day and 2 days before collecting urine samples (Table 1). For subjects who stayed indoors during the daytime, sunlight exposure time, ratio of sunlight-exposed skin area, and intensity of sunlight were regarded as zero. Smoking and drinking habits, age, sex, and body mass index (BMI; kg/m^2) were also included in the questionnaire as possible confounding factors. This study was approved by the Ethical Committee in Chubu University (approval no. 20008-5).

Measurement of levels of urinary 8-OHdG and skin pigmentation in the human study

Urine samples were frozen within 15 minutes after collection and kept at −80°C. An 8-OHdG ELISA kit (Nikken SEIL Co. Ltd.) and a creatinine kit (Cayman

Table 1. Criterion for each risk factor ($n = 127$)

Risk factors (total range)	Criteria
Sunlight-exposure time	
1 d before (0–6 h/d)[a]	$\geq$2 h/d
2 d before (0–10 h/d)[b]	$\geq$2 h/d
Ratio of sunlight-exposed skin area to the whole body	
1 d before (0–0.63)[a]	$\geq$0.2
2 d before (0–0.63)[b]	$\geq$0.2
Sunlight intensity	
1 d before (0–59.5 mW/cm^2)[a]	>30 mW/cm^2
2 d before (0–42.9 mW/cm^2)[b]	>30 mW/cm^2
L*-value (lightness)	
Sole (59.08–76.08)	$\geq$68
Forehead (49.52–66.29)	$\geq$63
Difference (sole minus forehead; −1.47 to 18.53)	<9
Sunscreen	
Never and irregular use or regular use	Regular use

[a]One day before the day of urine sample collection.
[b]Two days before the day of urine sample collection.

Chemical Company) were used according to the method previously described (17). Data of 8-OHdG were provided as creatinine-adjusted urinary 8-OHdG levels ($\mu g/$g creatinine). It is likely that age-related variations of renal function affect the creatinine-adjusted urinary 8-OHdG levels; in fact, age has been shown to affect creatinine-adjusted urinary 8-OHdG levels (18). The subjects in this study consisted of only young adults with intact renal function, thus minimizing the possible age-related effects on 8-OHdG levels. Skin pigmentation of sun-exposed (forehead) and -unexposed (sole) areas in each individual was evaluated as L*-values (lightness) by using a reflectance spectrophotometer (CR-400; Konica Minolta Sensing, Inc.) according to the previously described method (12, 19).

Statistical analysis in the human study

Statistical analysis was conducted following the method previously used (20). Total range and criteria in the risk factors examined in this study are summarized in Table 1. We carried out binary logistic regression analysis with creatinine-adjusted urinary 8-OHdG level (>8 $\mu g/g$ creatinine) as the dependent variable and sunlight exposure time per day (hours per day), ratio of sunlight-exposed skin area to the whole body, sunlight intensity (mW/cm^2), L*-value (lightness) in the skin, and regular use of full-spectrum (i.e., UVA and UVB) sunscreen as independent variables (Table 1). Models were adjusted for age, sex, smoking, drinking, and BMI because correlations between urinary 8-OHdG levels and these factors have been reported (18, 21–23). We used the SPSS (version 18) software package (SPSS Japan

Inc.) for these statistical analyses, and the significance level was set at $P < 0.05$.

Mice in the animal experimental study

HL-mice with melanin (Hos:HRM) developed by crossing hairless mice (Hos:HR-1) with C57BL/6J mice were purchased from Hoshino Laboratory Animals, Inc. HL-HPS-mice were developed by crossing an HL-mouse (Hos:HRM) with an RET-transgenic mouse of line 242 with the genetic background of C57BL/6J mice as shown previously (15). Control HL-mice (4 weeks old, $n = 20$) and littermate HL-HPS-mice ($n = 20$) were used. All mice were kept in a temperature- and humidity-controlled environment in the Animal Research Center of Chubu University. The Animal Care and Use Committee (approval nos. 18001 and 2210038) and Recombination DNA Advisory Committee (approval no. 06-01) in Chubu University approved this study.

Data collection in the animal experimental study

Single UVB (FL20S.E-30/DMR; spectral irradiance, 290–330 nm; peak wave, 305 nm; Toshiba Medical Supply Co. Ltd.) irradiation (45 mJ/cm^2) was carried out according to a method previously reported (15). Urine samples were collected at 24 hours before irradiation (control) and for 0 to 24 hours (days 0–1), 24 to 48 hours (days 1–2), and 48 to 72 hours (days 2–3) after irradiation. Analyses of levels of urinary 8-OHdG (μg/g creatinine), creatinine, and skin pigmentation in mice were carried out by the methods used in humans. Fontana–Masson staining for melanin-specific dyeing and hematoxylin and eosin (H&E) staining were carried out for morphologic analysis of the skin of mice.

Statistical analysis in the animal experimental study

Comparison of parameters before (control) and after (days 0–1, 1–2, and 2–3) UVB irradiation in each individual was carried out by the paired t test. Comparison of parameters in HL-mice (control) and HL-HPS-mice was made by the Mann–Whitney U test because data did not show a normal distribution.

Results

Effects of sunlight exposure–related factors on urinary 8-OHdG levels

We first examined whether sunlight-exposure time (hour per day) affects urinary 8-OHdG levels. There was no significant correlation between urinary 8-OHdG levels and time spent outdoors in the daytime on a sunny day both 1 day and 2 days before the day of urine sample collection (Table 2). There was also no significant correlation between urinary 8-OHdG levels and ratio of sunlight-exposed skin area to the whole body both 1 day and 2 days before the day of urine sample collection (Table 2).

We next examined whether sunlight intensity (mW/cm^2) affects urinary 8-OHdG levels. Interestingly, there

Table 2. Adjusted ORs for urinary 8-OHdG levels (≥ 8 μg/g creatinine, $n = 127$) and lifestyle

|	Adjusted OR (95% CI)
Sunlight-exposure time	
1 d before ($n = 29$)[a]	0.51 (0.15–1.71)
2 d before ($n = 53$)[b]	1.83 (0.69–4.85)
Ratio of sunlight-exposed skin area to the whole body	
1 d before ($n = 57$)[a]	0.93 (0.35–2.45)
2 d before ($n = 65$)[b]	0.62 (0.23–1.67)
Sunlight intensity	
1 d before ($n = 44$)[a]	4.35 (1.59–11.91)[c]
2 d before ($n = 54$)[b]	10.87 (3.17–37.36)[c]
L*-value (lightness)	
Sole ($n = 77$)	0.61 (0.23–1.62)
Forehead ($n = 13$)	12.17 (2.64–56.08)[c]
Difference ($n = 46$)	2.95 (1.02–8.48)[c]
Sunscreen	
Regular use ($n = 56$)	1.94 (0.32–11.77)

NOTE: Models were adjusted for age, sex, smoking, drinking, and BMI.
[a]One day before the day of urine sample collection.
[b]Two days before the day of urine sample collection.
[c]$P < 0.05$.

was a significant correlation (adjusted OR: 4.35) between urinary 8-OHdG levels (>8 μg/g creatinine) and sunlight intensity (>30 mW/cm^2) 1 day before collection of urine samples (Table 2). Further increase in adjusted ORs (10.87) was observed in the correlation between them 2 days before the day of urine sample collection (Table 2). To confirm the validity of our statistical model, we shifted the cutoff value of the dependent variable dichotomizing the urinary 8-OHdG levels from more than 3 to more than 9 μg/g creatinine and from more than 2 to more than 12 μg/g creatinine 1 day and 2 days before collection of urine samples, respectively. The results showed a significant correlation between urinary 8-OHdG levels and sunlight intensity on both days. We also shifted the cutoff value of the independent variable dichotomizing the intensity of sunlight exposure from more than 20 to more than 35 mW/cm^2 and from more than 30 to more than 35 mW/cm^2 1 day and 2 days before collection of urine samples, respectively. The correlation between them on both days before the measurement of 8-OHdG was likewise significant. These persistent results in different classifications showed that increase in sunlight intensity increases urinary 8-OHdG levels in humans. Because we have no data of time zone of the day when subjects were outdoors, average of sunlight intensity was used in this study. Further study is needed to more precisely clarify the effect of sunlight intensity on urinary 8-OHdG levels with evaluation of time-dependent change in sunlight intensity.
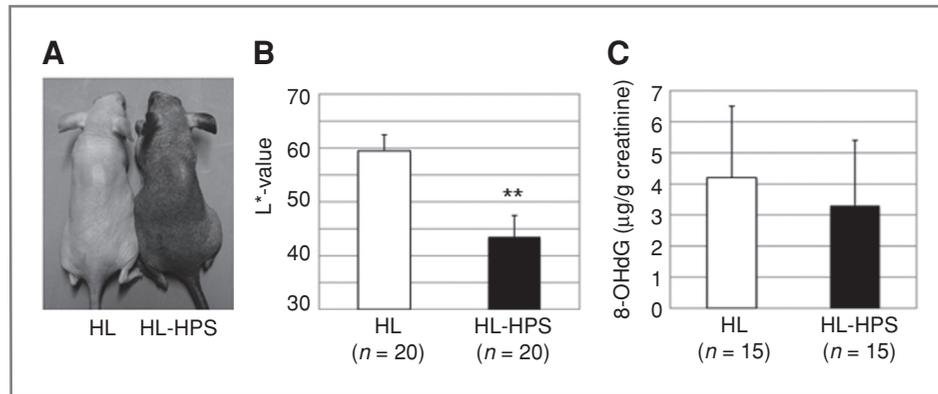
Figure 1. Constitutive characteristics in HL-mice and HL-HPS-mice. A, macroscopic characteristics of HL-mice (left) and HL-HPS-mice (right) are presented. B, L*-values (mean ± SD) evaluated by using a reflectance spectrophotometer in HL-mice and HL-HPS-mice are presented. Pigmented skin in HL-HPS-mice was confirmed by digital data. C, constitutive urinary 8-OHdG levels (mean ± SD) in HL-mice and HL-HPS-mice are presented. **, significantly different ($P < 0.01$) from the control by the Mann–Whitney U test.

Effects of skin pigmentation and sunscreen on urinary 8-OHdG levels

We next examined the effects of digitalized skin pigmentation (L*-value) levels on urinary 8-OHdG levels (Table 2). Previous studies showed that a reflectance spectrophotometer could be used to determine melanin density in the skin of humans and mice (12, 13, 19). High L*-values indicate low levels of cutaneous melanin density (14). In fact, the L*-value (mean ± SD = 68.94 ± 3.05) of the sole (sunlight-unexposed area) is higher than that (mean ± SD = 59.14 ± 3.28) of the forehead (sunlight-exposed area). There was a significant correlation (adjusted OR = 12.17) between urinary 8-OHdG levels (>8 μg/g creatinine) and L*-value of the forehead (>63) but not that of the sole (>68). To confirm the validity of our statistical model, we shifted the cutoff value of the dependent variable dichotomizing the urinary 8-OHdG levels from more than 6 to more than 8 μg/g creatinine. We also shifted the cutoff value of the independent variable dichotomizing the L*-value of the forehead from more than 63 to more than 65. The results showed a significant correlation between urinary 8-OHdG levels and L*-value of the forehead.

A significant correlation (adjusted OR = 2.95) between urinary 8-OHdG levels (>8 μg/g creatinine) and differences between L*-values in the sole and forehead (<9) was found. We shifted the cutoff value of the dependent variable dichotomizing the urinary 8-OHdG levels from more than 7 to more than 12 μg/g creatinine. We also shifted the cutoff value of the independent variable dichotomizing the differences between L*-values in the sole and forehead from less than 8 to less than 9. The results showed a significant correlation between urinary 8-OHdG levels and differences between L*-values in the sole and forehead.

There was no significant correlation between urinary 8-OHdG levels and regular use of sunscreen (Table 2). Our results suggest that the levels of urinary 8-OHdG are low in the subjects with pigmented skin but not in regular sunscreen users.
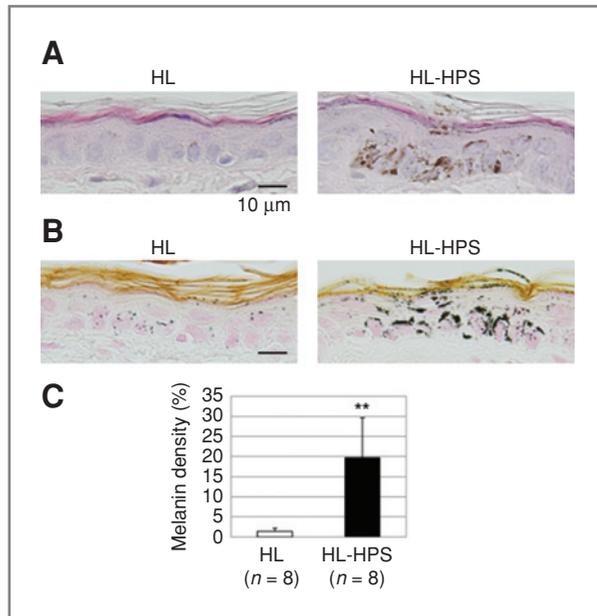
Characteristics of HL-mice and HL-HPS-mice

Macroscopic appearances of HL-mice and HL-HPS-mice are shown in Figure 1A. We noted highly pigmented skin in HL-HPS-mice. L*-values in the skin of HL-HPS-mice ($n = 20$) were significantly ($P < 0.01$) lower than those in control HL-mice ($n = 20$; Fig. 1B). There was no difference between urinary 8-OHdG levels in HL-mice ($n = 15$) and HL-HPS-mice ($n = 15$; Fig. 1C). No significant correlation was found between urinary 8-OHdG levels and cutaneous L*-values in HL-mice ($r^2 = 0.158$, $n = 14$) and HL-HPS-mice ($r^2 = 0.292$, $n = 14$) by Spearman's rank correlation test. These results indicated that levels of skin pigmentation do not affect the constitutive levels of urinary 8-OHdG.

Microscopic appearances of skin color in HL-mice and HL-HPS-mice are shown in Figure 2. Not only H&E staining (Fig. 2A) but also Fontana–Masson staining (Fig. 2B) showed high levels of melanin density in the epithelia from HL-HPS-mice compared with those in the epithelia from HL-mice. Epithelial melanin density in Fontana–Masson staining is shown in Figure 2C from calculation using the software program WinROOF (Mitani Corp.) following the method previously reported (24). These microscopic results showed that high density of melanin in the epithelium was involved in the macroscopically hyperpigmented skin in HL-HPS-mice.

Effects of UV irradiation on HL-mice and HL-RET-mice

Macroscopic appearances of HL-mice and HL-HPS-mice 2 days after UVB irradiation are shown in Figure 3A. UV-induced erythema was observed in HL-mice. The erythematous area in HL-mice ($n = 6$) was significantly ($P < 0.05$) larger than that in HL-HPS-mice ($n = 6$; Fig. 3B). Urinary 8-OHdG levels in HL-mice ($n = 13$) were
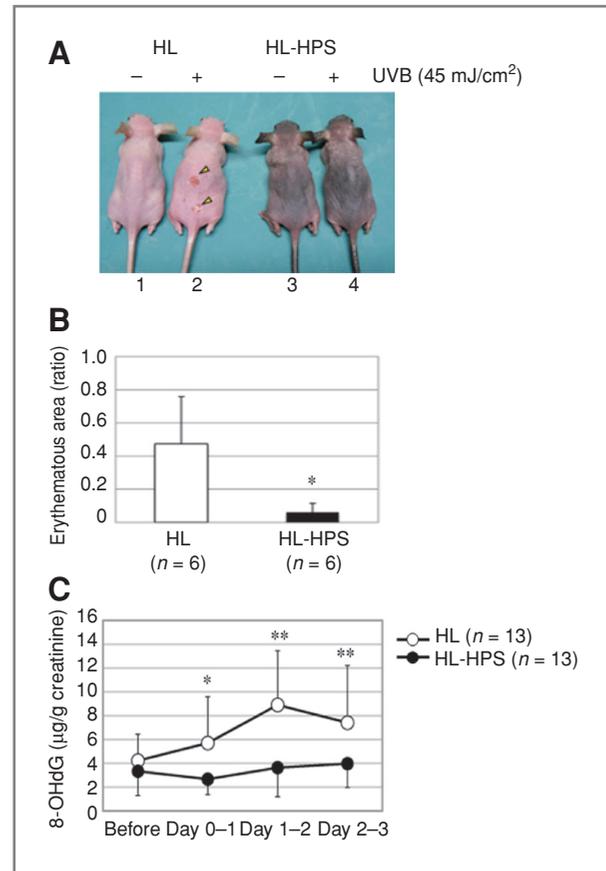
Figure 2. Histopathologic characteristics in HL-mice and HL-HPS-mice. H&E staining (A) and Fontana–Masson staining (B) of epithelia from HL-mice and HL-HPS-mice are presented. Melanin with brown color (right photograph in A) and black color (B) was detected. C, percentages (mean ± SD) of melanin density (melanin-containing area per measured area) in the epithelia from HL-mice and HL-HPS-mice were analyzed by the software program WinROOF after Fontana–Masson staining. **, significantly different ($P < 0.01$) from the control by the Mann–Whitney U test.

Figure 3. Effects of UV irradiation in HL-mice and HL-HPS-mice. A and B, macroscopic appearances of HL-mice (lanes 1 and 2 in A) and HL-HPS-mice (lanes 3 and 4 in A) before (lanes 1 and 3 in A) and 2 days after (lanes 2 and 4 in A) UVB irradiation (45 mJ/cm^2). UV-mediated erythematous lesions (arrow heads) are noted in HL-mice (lane 2 in A). Ratios (mean ± SD) of erythematous areas (erythematous areas per UV-irradiated area) in the skin from HL-mice ($n = 6$) and HL-HPS-mice ($n = 6$) were analyzed by the software program WinROOF (B). *, significantly different ($P < 0.05$) from the control by the Mann–Whitney U test. C, urinary 8-OHdG levels (mean ± SD) before and at 0 to 24 hours (days 0–1), 24 to 48 hours (days 1–2), and 48 to 72 hours (days 2–3) after UVB (45 mJ/cm^2) irradiation in HL-mice ($n = 13$) and HL-HPS-mice ($n = 13$) are presented. * and **, significantly different (*, $P < 0.05$; **, $P < 0.01$) by the paired t test.

maximally increased on days 1 to 2 after UV irradiation ($P < 0.01$) and were significantly higher on days 0 to 1 and days 2 to 3 after UV irradiation ($P < 0.05$) than those before UV irradiation (control). Because around 180 μW/cm^2 of UVB was detected in sunlight in our result, these results suggest that UVB corresponding to about 4 minutes of sunlight exposure significantly upregulated urinary 8-OHdG levels in mice 1 day and 2 days after the irradiation. On the other hand, no significant increase in urinary 8-OHdG levels after UV irradiation was observed in HL-HPS-mice ($n = 13$). These experimental results again suggest that urinary 8-OHdG levels are affected by skin pigmentation level.

Discussion

We showed that urinary 8-OHdG levels were increased by increase in sunlight intensity but not by increase in sunlight exposure time or sunlight-exposed skin area in human daily life. Urinary 8-OHdG levels were regulated by skin pigmentation but not by sunscreen. In HL-mice, urinary 8-OHdG levels were maximally increased 24 to 48 hours after UV irradiation. UV-mediated increase in urinary 8-OHdG levels was blocked in HL-HPS-mice. Thus, we have provided more reliable evidence of routine sunlight exposure–mediated DNA damage in humans through the combination of epidemiologic and experimental studies.

Unexpectedly, no significant correlation was found between urinary 8-OHdG levels and sunlight exposure time in this study. We further analyzed the correlations of urinary 8-OHdG levels with the amount of sunlight exposure (J/cm^2) [= multiplication of sunlight intensity (mW/cm^2) and sunlight-exposure time (seconds)] with consideration of the confounding factors as shown in the Methods section. There was a significant correlation between urinary 8-OHdG levels (>8 μg/g creatinine) and amount of sunlight exposure (>100 J/cm^2) 2 days before collection of urine samples (OR = 4.62; CI = 1.40–15.26). However, no significant correlation was found between them 1 day before collection of urine samples (OR = 2.02; CI = 0.76–5.36). The OR (4.62) of urinary 8-OHdG levels (>8 μg/g creatinine) and amount of sunlight

exposure (>100 J/cm^2) were lower than those (10.87) of urinary 8-OHdG levels (>8 μg/g creatinine) and sunlight intensity (>30 mW/cm^2) 2 days before collection of urine samples. Our experimental results showed that UVB irradiation corresponding to only 4 minutes of sunlight exposure significantly upregulated urinary 8-OHdG levels in HL-mice. Together with results of previous studies showing that UVB upregulated levels of transcript expression and activity of signal transduction molecules in the skin within minutes in humans (4, 25), we speculate that the trigger event for 8-OHdG production starts and reaches plateau level within minutes of sunlight exposure. The results of our study showing no correlation between sunlight exposure time and urinary 8-OHdG levels might be due to the fact that we evaluated sunlight exposure in hours and not in minutes.

No correlation was found between urinary 8-OHdG levels and sunlight-exposed skin area in our human study. Further analysis showed that there were no correlations between urinary 8-OHdG levels and amount of sunlight exposure with consideration of sunlight-exposed skin area (J/cm^2) [= multiplication of sunlight intensity (mW/cm^2), sunlight-exposure time (seconds) and ratio of sunlight-exposed skin area to the whole body] 1 day and 2 days before collection of urine samples. Because all of the subjects who went outdoors suffered from sunlight exposure at least on the face, these results suggest that exposure of the face to sunlight is sufficient to increase urinary 8-OHdG levels.

L*-values obtained by using a reflectance spectrophotometer have been used as a digital marker of melanin density in the skin of Asians (14). L*-values of a sunlight-unexposed area (sole) are thought to correspond to the constitutive cutaneous melanin density in each individual, and L*-values of a sunlight-exposed area (forehead) are thought to correspond to the sunlight-mediated increase in cutaneous melanin density in addition to the constitutive melanin density. Therefore, the difference between L*-values in the sole and forehead correspond to the increased cutaneous melanin density in response to sunlight. Our results showed that urinary 8-OHdG levels were correlated with not only L*-values of the forehead but also the difference between L*-values in the sole and forehead. These results suggest that increase in melanin density induced by sunlight irradiation protects against increase in 8-OHdG levels. These results also indirectly suggest that sunlight exposure in our daily life is involved in the levels of DNA damage via modulation of skin pigmentation levels.

There are 2 possible mechanisms for the regulation of urinary 8-OHdG levels by cutaneous melanin. One is via the antioxidative effect and the other is via physical block of sunlight (26, 27). There was no significant correlation between urinary 8-OHdG levels and constitutive cutaneous melanin density (L*-values of the sole) in the subjects. There was also no difference between urinary 8-OHdG levels in mice with normal pigmentation (HL-mice) and mice with hyperpigmentation (HL-HPS-mice).

No statistical correlation between urinary 8-OHdG levels and cutaneous L*-values in both HL-mice and HL-HPS-mice was found. Our results suggest that cutaneous melanin–mediated physical block of sunlight rather than a melanin-mediated antioxidative effect plays an important role in the regulation of urinary 8-OHdG levels.

It has been reported that sunscreen is useful for prevention of skin cancer such as squamous cell carcinoma as well as prevention of suntan and sunburn (28, 29). However, there has been no report on the effects of sunscreens on DNA damage caused by increase in 8-OHdG levels in humans or mice. Although we anticipated that urinary 8-OHdG levels would be decreased in regular sunscreen users, there was no difference between urinary 8-OHdG levels in sunscreen users and nonusers in our study. Further study that includes more information on sunscreen such as application frequency per day and intensity for UVA and UVB is needed to more precisely clarify the effect of sunscreen on urinary 8-OHdG levels.

8-OHdG is thought to be a critical biomarker of carcinogenesis and oxidative DNA damage (1, 2). We previously showed a protective effect of hairless mice with hyperpigmented skin on UV-mediated skin cancer (15). Therefore, our results suggest a high risk of developing skin cancer in humans with low cutaneous melanin density. Urinary 8-OHdG levels and cutaneous L*-values might become useful biomarkers for predicting the risk of developing skin cancer such as after administration of minimal erythema dose (MED), the correlations among urinary 8-OHdG levels, cutaneous L*-values, and development of skin cancers have been revealed by further study.

In summary, we found novel correlations among sunlight intensity, cutaneous melanin density, and DNA damage by a human epidemiologic study. Some of the findings were reinforced by an animal experimental study.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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