Effects of Sunscreens and a DNA Excision Repair Enzyme on Ultraviolet Radiation–Induced Inflammation, Immune Suppression, and Cyclobutane Pyrimidine Dimer Formation in Mice

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Exposure of skin to ultraviolet (UV) radiation inhibits the induction of delayed-type hypersensitivity (DTH) responses initiated at a distant, unirradiated site. Recent studies attributed this form of immune suppression to DNA damage in the form of cyclobutane pyrimidine dimers (CPD). In the present study, we investigated the protective defects of sunscreens on UV-induced systemic suppression of DTH to *Candida albicans,* inflammation, and DNA damage. The photoprotective effects of sunscreen preparations containing 8% octyl-N-dimethyl-p-aminobenzoate, 7.5% 2-ethylhexyl-p-methoxycinnamate, or 6% benzophenone-3 were studied in C3H mice exposed to a single dose of 500 mJ/cm² UVB radiation from FS40 sunlamps. Inflammation was determined by the amount of skin edema at the site of UV irradiation, and DNA damage was assessed by measuring the frequency of endonuclease-sensitive sites in the epidermis. Application of the sunscreens before UV irradiation gave 75–97% protection against UV-induced edema, 67–91% protection against formation of CPD, but only 30–54% protection against suppression of DTH. In contrast, the topical application of liposomes containing a CPD-specific DNA repair enzyme immediately after UV irradiation resulted in 82% protection against suppression of DTH, but at best, 39% protection against skin edema. These findings demonstrate that sunscreens give less protection against UV-induced immune suppression than against skin edema and CPD formation. Furthermore, they suggest that less DNA damage is required to cause UV-induced immune suppression than to cause sunburn. Key words: delayed-type hypersensitivity/DNA damage/liposomes. *J Invest Dermatol 101:523–527, 1993*

Exposure of skin to ultraviolet (UV) radiation induces various biologic alterations including immune suppression [1]. A variety of immune responses such as contact hypersensitivity (CHS) and delayed-type hypersensitivity (DTH) reactions are impaired after UV irradiation. The immune suppression induced by UV radiation plays a critical role in the pathogenesis of skin cancers in mice [2,3]. Evidence is accumulating that immunologic effects of UV radiation may also contribute to the development of skin cancer in humans [4–6]. Furthermore, immune suppression by UV radiation may increase the severity of certain infectious diseases. For instance, it was demonstrated that exposure of mice to UV radiation abrogated DTH responses to Herpes simplex virus type I and II [7,8], *Candida albicans* [9], *Leishmania major* [10], and *Mycobacterium bovis* [11].

Immune suppression by UV radiation is associated with the presence of T-suppressor lymphocytes [3]. The mechanisms by which UV radiation activate the suppressor pathway are not completely known, but the release of soluble mediators such as prostaglandins [12], tumor necrosis factor-α [13], interleukin (IL)-1 [12], contra IL-1 [14], and IL-10 [15] has been implicated. In addition, urocanic acid in the stratum corneum has immunosuppressive properties, particularly after isomerization to its *cis*-form by UV irradiation [16]. On the molecular level, however, DNA damage in the form of cyclobutane pyrimidine dimers (CPD) appears to be the primary trigger for systemic immune suppression by UV radiation [17,18].

Sunscreens prevent UV-induced DNA damage [19–21], and they are highly protective against sunburn in humans and against UV-induced skin aging [22], and tumor initiation [23] and promotion [24] in animals. However, the evidence that sunscreens protect against the immunosuppressive effects of UV radiation has been controversial. Indeed, in a number of studies sunscreens did not protect experimental animals [25–28] and humans [29,30] from a variety of UV effects on the immune system. These results are difficult to reconcile with the notions that sunscreens reduce DNA damage and that DNA damage is responsible for UV-induced immune suppression. Therefore, we undertook a study to determine whether the effect of sunscreens on immune suppression correlated with their ability to prevent DNA damage.

In this study, we investigated the effects of three sunscreen compounds on UV-induced immune suppression, inflammation, and DNA damage in mice. The immunoprotective ability of the sunscreens was studied in a model of UV-induced systemic suppression of DTH to *C. albicans* [9]. Skin edema was used as the measure of UV-induced inflammation, and DNA damage was assessed by mea-

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Abbreviations: CHS, contact hypersensitivity; CPD, cyclobutane pyrimidine dimer(s); 2-EHMC, 2-ethylhexyl-p-methoxy-cinnamate; o-PABA, octyl-N-dimethyl-p-aminobenzoate; SPF, sun-protection factor.

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suring the number of CPD in the epidermis using the endonuclease-sensitive site assay [31]. The sunscreen preparations contained octyl-N-dimethyl-p-aminobenzoate (o-PABA), 2-ethylhexyl-p-methoxy-cinnamate (2-EHMC), or benzophenone-3.

In addition, we studied the effect of liposomes containing T4 endonuclease V, a CPD-specific DNA excision repair enzyme, on UV-induced inflammation and suppression of DTH to *C. albicans.* When topically applied to skin, these T4N5 liposomes penetrate cells of the epidermis, deliver the endonuclease intracellularly, and increase the rate of CPD repair in DNA [32]. Topical application of T4N5 liposomes abrogates suppression of DTH and CHS responses in C3H mice [18] and reduces UV-induced skin cancer formation in hairless mice [32]. We used this approach to analyze the role of CPD in UV-induced inflammation and suppression of DTH.

MATERIALS AND METHODS

Animals Specific-pathogen-free female C3H/HeNCr(MTV$^-$) mice were supplied by the Animal Production Area of the Frederick Cancer Research Facility (Frederick, MD) or Charles River Breeding Laboratories (Wilmington, MA). The mice were housed in a pathogen-free barrier facility accredited by the American Association for Accreditation of Laboratory Animal Care, in accordance with current US Department of Agriculture, Department of Health and Human Services, and National Institutes of Health (NIH) regulations and standards. All animal procedures were approved by the Institutional Animal Care and Use Committee. The mice were given free access to NIH formula 31 mouse chow and sterilized water. Ambient lighting was controlled to provide a regular 12-h light/12-h dark cycle. Eight- to 16-week-old, age-matched mice were used in the experiments.

Sunscreens The sunscreen compounds were supplied by ISP Van Dyk Inc. (Belleville, NJ); the preparations used on animals contained 8% o-PABA, 7.5% 2-EHMC (both UVB absorbers), or 6% benzophenone-3 (UVA + UVB absorber) in an oil-in-water emulsion. Their transmission spectra were reported in a previous study [33], in which both UVB sunscreens gave an "anti-inflammatory" sun-protection factor (SPF) of at least 8, and the benzophenone-3–containing sunscreen gave an SPF of at least 4 in C3H mice. To study the photoprotective properties of the sunscreen preparations, they were liberally applied (approximately 200–250 μl per mouse) and rubbed on the shaved dorsal skin and tail of the mice 20 min before UV irradiation.

T4N5 Liposomes T4N5 liposomes were prepared by encapsulating purified, recombinant T4 endonuclease V in liposomes composed of phosphatidylcholine, phosphatidylethanolamine, oleic acid, and cholesterol hemisuccinate (2:2:1:5 molar ratio) by the detergent dialysis method [34]. The concentration of the entrapped enzyme was determined by enzyme-linked immunosorbent assay [35] and expressed as μg T4 endonuclease V per ml of vehicle. The encapsulated activity was assayed by nicking of UV-supercoiled DNA, with and without dissolution of the liposomes [35]. Control preparations of liposomes contained boiled (enzymatically inactive) T4 endonuclease V [34]. The liposomes were mixed into a 1.5% hydrogel (Carbopol-941; BF Goodrich) made with phosphate-buffered saline and applied to mouse skin with a moist cotton swab. Immediately after UV irradiation, 250 μl of liposome suspension containing 0.5 μg/ml T4 endonuclease V was applied to the UV-irradiated dorsal skin and tail of the mice.

UV Irradiation UV radiation was provided by a bank of six FS40 sunlamps (National Biological Corp, Twinsburg, OH), which have a peak emission at 313 nm and deliver 65% of their total energy within the UVB (280–320 nm) wavelength range; their UVB irradiance was 0.5 mW/cm^2 at a 20-cm distance, as determined by an IL 700 radiometer equipped with an SEE 240 detector fitted with an SES280 filter and a W2372 quartz diffuser (International Light, Inc., Newburyport, MA). One day before UV irradiation, the dorsal fur of the mice was shaved with electric clippers, and the animals were placed in individual compartments in cages located 20 cm below the light source. Because of shielding by the cage lids, the final irradiance received by the animals was approximately 0.3 mW/cm^2. Mice were exposed to a single dose of 500 mJ/cm^2 UVB, which is approximately five times the minimal dose required to elicit edema on dorsal skin of C3H mice [33]. Except for exposure to UV radiation, control mice were treated exactly the same as the UV-irradiated mice.

Measurement of Inflammation Prior to this study, we found that measurement of skin swelling, which is primarily due to skin edema, is a more sensitive and reproducible method to determine UV-induced inflammation than visual evaluation of erythema (unpublished data). Therefore, we used skin swelling as our measure for inflammation. The double-skin-fold thickness of the dorsal skin of the mice was measured with a spring-loaded micrometer (Mitutoyo, Tokyo, Japan) prior to and 24 h after UV exposure. Skin edema was determined by subtracting the average skin thickness before UV irradiation, which ranged from 0.7–0.9 mm, from that after UV irradiation. In some experiments, application of the sunscreens or the vehicle alone resulted in a small amount of skin swelling. Therefore, net skin edema was determined by subtracting the skin swelling of sunscreen-treated, unirradiated mice from that of sunscreen-treated, UV-irradiated mice.

DTH Response Formalin-fixed *C. albicans* was prepared as described previously [9]. Mice were sensitized by injections of 100 μl of formalin-fixed *C. albicans* cells (1×10^7) subcutaneously (sc) into each flank. Nine days later, the hind-footpad thickness was measured with a micrometer, and the animals were challenged by intradermal injection of 50 μl of *Candida* antigen (Antigen Supply House, Northridge, CA) in both hind footpads. Footpad thickness was measured again 24 h later, and the swelling was determined by subtracting prechallenge (1.7–2.0 mm) from postchallenge measurements. Specific footpad swelling was calculated by subtracting the average footpad swelling of mice receiving the challenge dose only from that of mice given both the sensitizing and challenge doses. The percent suppression of DTH was determined by the following formula: $[1 - (A/B)] \times 100$, where A represents the specific footpad swelling in sensitized and UV-irradiated mice, and B represents that in sensitized, unirradiated mice.

Assay for CPD The frequency of CPD in epidermal DNA was determined by the endonuclease-sensitive site assay using alkaline agarose gels [31]. Mice were killed by cervical dislocation immediately after UV exposure and the epidermis of excised dorsal skin was isolated by overnight digestion in 0.25% trypsin on ice, and the DNA was purified by two rounds of proteinase K digestion (100 mg/ml in 1% sodium dodecylsulfate, 37°C for 30 min); phenol, phenol/chloroform (1 : 1 v/v), and chloroform extraction; and ethanol precipitation. The DNA was then treated with purified T4 endonuclease V (10 μg/ml) to produce breaks at all CPD sites, and the single strands were separated by alkaline agarose gel electrophoresis. Images of the ethidium bromide-stained gels were digitized by a Star I CCD camera (Photometrics, Tucson, AZ) and the frequency of endonuclease-sensitive sites (i.e., CPDs) was calculated from the size of distribution of the DNA in each lane analyzed by Optimus software (Biosoft, Seattle, WA), as described [36]. The average number of CPD per unit length of DNA in skin was determined from samples of four mice per experimental group.

Statistics The significance of differences in skin edema, DTH responses, and DNA damage between different experimental groups was determined using Student two-tailed t test. Each experimental group contained at least five mice. A difference was considered to be statistically significant when $p \leq 0.05$.

The percent protection against UV-induced skin edema, suppression of DTH, and CPD formation by a treatment with sunscreen or liposome suspension was determined by the following formula: $[1 - (T/U)] \times 100$, where T is the treated, UV-irradiated group and U is the untreated, UV-irradiated group.

RESULTS

Effect of Sunscreens on UV-Induced Suppression of DTH

Exposure of mice to UV radiation inhibits the induction of the DTH response to *C. albicans* injected sc at an unirradiated site. To

Table I. Effect of Sunscreens on Suppression of DTH to *C. Albicans*

Treatment	Footpad Swelling ± SEM (× 0.01 mm)	Net Footpad Swelling	% Suppression[a]	% Protection[a]
None	22.3 ± 0.5			
Sens	37.8 ± 4.8	15.5		
UV + Sens[b]	22.9 ± 2.0	0.6	96[c]	
UV + o-PABA + Sens	31.3 ± 1.6	9.0	42	56[d]
UV + 2-EHMC + Sens	28.1 ± 1.3	5.8	63	34
UV + BP-3 + Sens	25.5 ± 0.7	3.2	79[c]	18
UV + Vehicle + Sens	20.8 ± 1.2		100[c]	0

[a] % suppression and % protection as defined in *Materials and Methods.*
[b] Sens, sensitized with *C. albicans;* UV, 500 mJ/cm^2 UVB; n = 5.
[c] $p \leq 0.05$ versus Sens.
[d] $p \leq 0.05$ versus UV + Sens.

investigate the effect of sunscreens on this form of UV-induced immune suppression, groups of mice were exposed to a single dose of 500 mJ/cm² UVB, and the DTH response to *C. albicans* and the formation of CPD in murine epidermis were measured. To rule out the possibility that the topical application of a sunscreen or the vehicle might itself interfere with DTH to *C. albicans*, initial experiments were performed with all the necessary control groups. The application of sunscreen or vehicle alone had no significant effect on the induction or elicitation of DTH in unirradiated mice or on the background footpad swelling reaction in unsensitized mice (data not shown).

Table I shows the results of one experiment evaluating the effects of the sunscreens on UV-induced systemic suppression of DTH to *C. albicans*. In this experiment, exposure of mice to 500 mJ/cm² UVB significantly reduced the DTH response, by 96%. The topical application of sunscreens before UV irradiation partially protected against suppression of DTH, by 56% (o-PABA), 34% (2-EHMC), and 18% (benzophenone-3). The mean percent suppression of DTH by UV radiation and the mean percent protection by the sunscreens from four separate experiments is presented in Fig 1*A*. The protection ranged widely, from 18 to 94% for o-PABA, from 7 to 47% for 2-EHMC, and from 14 to 72% for benzophenone-3; the vehicle did not protect against suppression of DTH in any experiment.

Effect of Sunscreens on UV-Induced Inflammation As shown in Fig 1*B*, exposure of mice to 500 mJ/cm² UVB resulted in significant skin edema at 24 h after UV irradiation. In contrast to their partial and variable effect on UV-induced suppression of DTH, the topical application of sunscreens provided consistent and effective protection against UV-induced edema in all experiments. The o-PABA– and 2-EHMC–containing preparations completely protected against the UV-induced inflammatory response, as there was no significant edema in o-PABA– and 2-EHMC–treated mice compared to sunscreen-treated, unirradiated mice. The benzophenone-3–containing preparation only partially protected against the UV-induced inflammation; nevertheless the amount of edema was significantly less than that in unprotected, UV-irradiated mice. The vehicle had no protective activity against UV-induced skin edema.

Effect of Sunscreens on UV-Induced Formation of CPD The exposure of mice to 500 mJ/cm² UVB resulted in the formation of CPD in unprotected murine skin (Fig 1*C*), whereas no CPD were observed in unirradiated mouse skin (data not shown). Topical application of sunscreens reduced the number of CPD by 91% (o-PABA), 86% (2-EHMC), and 67% (benzophenone-3); the vehicle had no detectable protective effect (Fig 1*C*).

Effect of T4N5 Liposomes on UV-Induced Suppression of DTH and Inflammation The topical application of T4N5 liposomes immediately after UV irradiation was highly effective in protecting against UV-induced suppression of the induction of DTH to *C. albicans*. As shown in Table II, the T4N5 liposomes almost completely abrogated the suppression of DTH to *C. albicans*; the observed footpad-swelling response in mice treated with T4N5 liposomes after UV irradiation did not differ statistically from the response of the T4N5-treated, unirradiated mice. In contrast, liposomes containing heat-inactivated endonuclease had no significant effect on suppression of DTH to *C. albicans*. This result confirms those obtained in a previous study [18].

The skin edema data from the experiment shown in Table II are presented in Fig 2. In contrast to their highly protective effect on UV-induced suppression of DTH, the topical application of T4N5 liposomes immediately after UV irradiation did not provide effective protection against edema formation. In this particular experiment, the T4N5 liposomes diminished the inflammatory response induced by 500 mJ/cm² UVB, but did not prevent it. In four separate experiments, the application of T4N5 liposomes gave a mean ± SEM protection of 17 ± 9% (range, 0–39%) against UV-

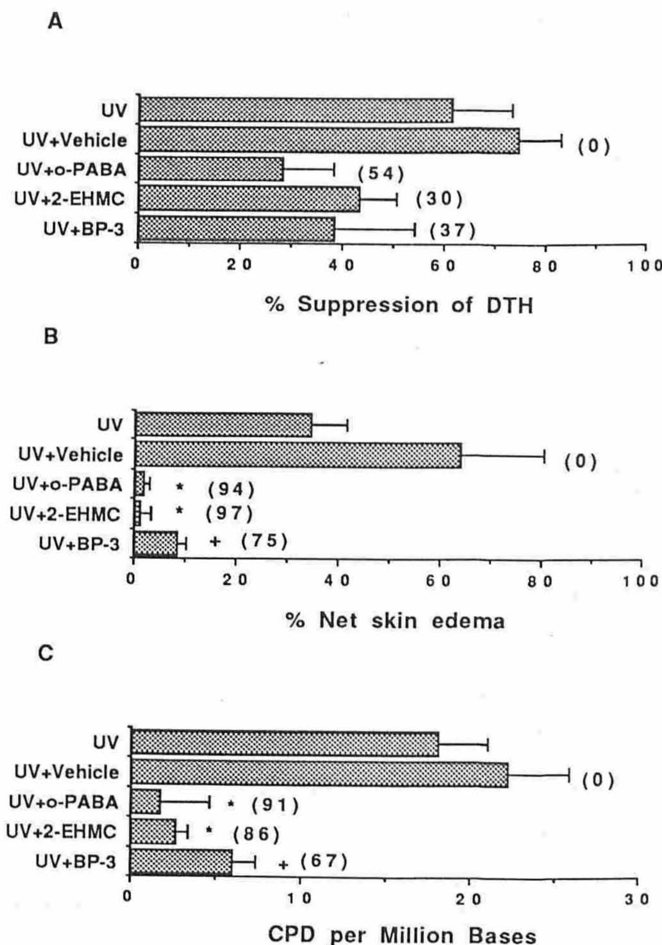

Figure 1. The effects of sunscreens on UV-induced systemic suppression of DTH to *C. albicans*, inflammation, and DNA damage (*UV*, 500 mJ/cm² UVB; *values in parentheses*, percent protection by a sunscreen, as defined in *Materials and Methods*). *A)* Systemic suppression of DTH to *C. albicans*. The mean percent suppression ± SEM, as calculated from four separate experiments is given. *B)* Inflammation as measured by skin edema 24 h after UV irradiation. The average percent net skin edema of original double-skin-fold thickness from four experiments is shown (data are mean ± SEM, $^*p \leq 0.005$ and $^\dagger p \leq 0.05$ versus unprotected, UV-irradiated group). *C)* DNA damage as measured by the frequency of CPD. Groups of mice were killed immediately after UV irradiation and DNA from the epidermis was analyzed for CPD by the endonuclease sensitive-site assay ($n = 4$, data are mean ± SEM, $^*p \leq 0.0005$ and $^\dagger p \leq 0.005$ versus unprotected, UV-irradiated group).

induced skin edema formation. Applying liposomes containing heat-inactivated endonuclease did not significantly affect the UV-induced edema formation.

DISCUSSION

In this study, the sunscreen preparations containing o-PABA, 2-EHMC, or benzophenone-3 effectively protected C3H mice against UV-induced inflammation and against CPD formation in the epidermis. As expected from their *in vitro* transmission spectra [33], both UVB sunscreens gave approximately equal photoprotection against UV-induced skin edema and CPD formation, and the benzophenone-3–containing preparation was less effective in preventing these effects of UV radiation. The sunscreens also gave some protection against UV-induced systemic suppression of the induction of DTH to *C. albicans*. However, the immunoprotective ability of the sunscreens was highly variable, limited, and inferior to their ability to protect against inflammation as measured by skin

Table II. Effect of T4N5 Liposomes on Suppression of DTH to *C. Albicans*

Treatment	Footpad Swelling ± SEM (× 0.01 mm)	Net Footpad Swelling	% Suppression[a]	% Protection[a]
None	13.2 ± 1.2			
Sens[b]	30.0 ± 2.8	16.8		
HI + Sens[b]	25.5 ± 3.2	12.3	27	
T4N5 + Sens[b]	28.2 ± 0.7	15.0	11	
UV + Sens[b]	14.0 ± 1.4	0.8	95[c]	
UV + HI + Sens[b]	17.8 ± 2.0	4.6	73[c]	23
UV + T4N5 + Sens	27.2 ± 5.4	14.0	17	82[d]

[a] % suppression and % protection as defined in *Materials and Methods*.
[b] Sens, sensitized with *C. albicans;* HI, liposomes containing heat-inactivated endonuclease; T4N5, liposomes containing active endonuclease; UV, 500 mJ/cm^2 UVB; n = 5.
[c] $p \leq 0.01$ versus Sens.
[d] $p \leq 0.05$ versus UV + Sens.

edema. The results indicate that UV-induced suppression of DTH is less sensitive to the photoprotective effects of sunscreens than inflammation. This agrees with a recent study from our laboratory in which these sunscreens exhibited a moderate and variable ability to prevent UV-induced suppression of CHS [33]. In dose response studies across a broad range of UV doses, these sunscreens protected C3H mice against systemic suppression of CHS to 2,4-dinitrofluorobenzene, but only at low UV doses and again not as well as they protected against inflammation [33]. Although the reasons for the variability in protection against UV-induced immune suppression by sunscreens remain unclear at present, this variability seems to be characteristic for sunscreens because it was not observed with T4N5 liposomes.

Our finding that sunscreens have immunoprotective ability agrees with certain other studies, in which PABA [37–39] and 2-EHMC [40] protected against UV-induced systemic suppression of CHS and induction of tumor susceptibility in rodents, and not with others [25–30]. Differences in methodology (i.e., UV light source, number of treatments, UV dose, sunscreen formulation, and application) could account for the discrepancy between those studies and ours. For instance, most previous studies [25–30] involved chronic UV treatment regimens, whereas we used a single UV exposure. The UV dose seems to be a critical factor in determining whether sunscreens are immunoprotective [33]. Thus, a high cumulative UV dose alone may explain why immunoprotection was not observed in any of those studies [25–30].

Our findings that sunscreens protected against formation of CPD is in agreement with an earlier report [20]. To the best of our knowledge, however, the relation between photoprotection against DNA damage and the immunologic effects of UV radiation was not studied previously. Recently, UV-induced systemic suppression of DTH to *C. albicans* was attributed to DNA damage in the form of CPD in the epidermis, based on the ability of T4N5 liposomes to increase repair of CPD and prevent immune suppression [18]. Because the topical application of our sunscreen preparations reduced formation of CPD in the epidermis, protection was expected against suppression of DTH. Indeed, some immune protection was observed, but it was highly variable and incomplete, whereas UV-induced inflammation was consistently prevented by the application of sunscreens.

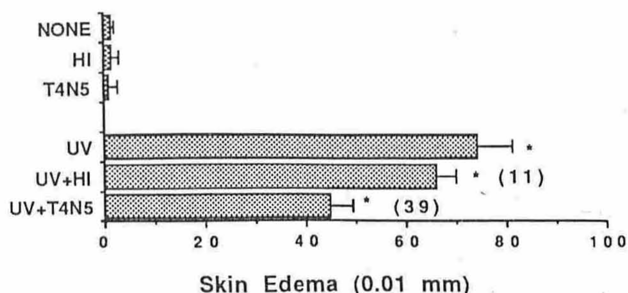

Figure 2. The effect of T4N5 liposomes on UV-induced inflammation as measured by skin edema 24 h after UV irradiation (*UV*, 500 mJ/cm^2 UVB; *HI*, liposomes containing heat-inactivated endonuclease; *T4N5*, liposomes containing active endonuclease; n = 5, data are mean ± SEM, *$p \leq 0.001$ versus unirradiated groups; values in parentheses represent percent protection by the treatment with liposomes, as defined in *Materials and Methods*.

Several interpretations are possible to explain this discrepancy. First, UV-induced edema may require many CPD per cell, whereas immune suppression may need only a small number of CPD. Second, there may be a nonuniform distribution and repair of CPD in epidermal cells, and the target cell for immune suppression may be different from the target cell for inflammation. Third, sunscreens themselves may induce immune suppression; for instance, they may chemically interact with DNA [41] and consequently initiate immune suppression. Fourth, other mechanisms unrelated to CPD formation may also play a role in UV-induced inflammation. For instance, cell-membrane damage [42], as well as DNA damage [43–45], may be important in UV-induced inflammation. Sunscreens may block such a mechanism more efficiently than formation of CPDs, and therefore may also provide better protection against UV-induced inflammation than against immune suppression.

In contrast to the sunscreens, the application of liposomes containing the T4 endonuclease V, a CPD-specific DNA repair enzyme, almost completely protected mice from UV-induced systemic suppression of DTH, whereas the UV-induced inflammatory response was only partially affected. The finding that the repair of UV-induced DNA damage prevents immune suppression is consistent with the results of studies carried out in the South American opossum *Monodelphis domestica* [17]. However, in *M. domestica* other effects of UV radiation including erythema and edema were also almost completely prevented by the photoreactivating enzyme [43–45]. This difference from our study may be due to differences in the rates of UV-induced inflammation and immune suppression and excision and photoreactivation repair. Inflammation is a rapid effect of UV radiation, occurring within a few hours after UV exposure. In contrast, immune suppression is not evident until 3 d after UV irradiation. DNA repair by photoreactivation is a rapid process [17], whereas enhanced DNA repair by topical application of T4N5 liposomes seems to occur more slowly [18]. One hour after UV exposure, photoreactivation by means of visible light had reduced the number of CPD to approximately 15% in opossums [17], whereas 6 h after UV exposure, T4N5 liposomes had reduced the number of CPD to only 40–50% of that in UV-irradiated, untreated mice [18]. Thus, that T4N5 liposomes only partially affected UV-induced edema may be due to the relatively slow repair rate. Other mechanisms that may also play a role in UV-induced inflammation would presumably not be affected by T4N5 liposomes.

Several conclusions may be drawn from this study. First, immune suppression and inflammation are different effects of UV radiation and involve different mechanisms. Second, the immunoprotective ability of sunscreens is limited and inferior to their ability to protect against UV-induced inflammation and formation of CPD. Therefore, the use of sunscreens may protect subjects from the immunosuppressive effects of UV irradiation only as long as it does not encourage them to prolong their sunlight exposure. After excessive sunlight exposure, immunosuppressive effects and their negative biologic consequences might occur despite complete sunscreen protection from sunburn. Third, these studies suggest that topical application of liposomes containing T4 endonuclease V after UV irradiation may be more effective in protecting against immune suppression than the application of sunscreens before UV irradiation. However, we speculate that sunscreens and T4N5 liposomes

may have additive protective abilities against the immunologic effects of UV radiation. Therefore, sunscreen use before UV exposure and the application of liposomes to deliver lesion-specific repair enzymes to the skin *in situ* afterwards may be a useful way to further reduce the immunosuppressive and carcinogenic effects of UV radiation.

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