strongly suppressed UV-induced tumor formation and growth than SPF 10 sunscreen even in (-/-) mice. This may be mainly due to stronger protection against CPD formation after UVR with SPF 60 sunscreen. Mutations of the p53 tumor suppressor gene are now considered to be a key component of UV-induced cancer development. Most of sunlight-induced human skin cancers and UV-induced murine tumors contain p53 mutations at dipyrimidine sites. The skin tumor of XP patients also reveal p53 mutations with a UV-specific pattern (Dumaz, 1993) (Sato, 1993) (Matsumura, 1995). Although the XP patients examined in these studies included different complementation groups, the similar p53 mutations were detected in UV-induced skin tumors of XPA-deficicent mice (Takeuchi, 1998). Ananthaswamy *et al* demonstrated that topical application of sunscreens protected mice against UV-induced p53 mutations and also against skin cancers (Ananthaswamy, 1997, 1999).

It is generally accepted that UV-induced immunosuppression also plays a crucial role in the development of non melanoma skin cancers. However, previous studies reported that sunscreens that completely prevented UV-induced inflammation were not necessarily effective in preventing UV-induced immunosuppression. Wolf *et al* reported that sunscreens gave complete protection against inflammation and local suppression of contact hypersensitivity in C3H mice, but were less effective in protecting against local immunosuppression (Wolf, 1993). In the present study, SPF 60 sunscreen partially protected against local immunosuppression, but not against systemic immunosuppression in (-/-) mice. It seems likely that protective effect of sunscreens against UV-induced immunosuppression is less satisfactory in (-/-) mice than in (+/+) mice, because immunosuppresion is greatly enhanced in (-/-) mice (Miyauchi-Hashimoto, 1996).

XP patients develop accelerated photoaging, including dry skin (xeroderma), hyperpigmentation (pigmentosum), hypopigmentation and wrinkling at an early age. Our data demonstrated that photoaging was also induced more easily by UVB irradiation in (-/-) mice than in (+/+) mice. This indicates that the defect in nucleotide excision repair is

involved in the enhanced photoaging of XP patients. SPF 10 sunscreen provided unsatisfactory protecting ability against photoaging compared with SPF 60 sunscreen in (-/-) mice. This finding is in marked contrast to the previous study which indicated that SPF 15 sunscreen provides satisfactory protection against photoaging in mouse model (Uitto, 1998). Because photoaged skin contains populations of mutated cells but have not been removed by the immunologic surveillance systems (Yaar, 1998), protection against enhanced photoaging in (-/-) mice may also lead to prevent skin cells from malignant changes. Collectively, higher SPF sunscreen is recommended for protecting XP patients against photoaging that is needed for healthy person.

Sunscreens are designed primarily to protect against UVB irradiation, and SPF value does not reflect protective ability against UVA irradiation. Acute UV-inflammation is induced mainly by UVB radiation. However, UVA range is also responsible for DNA damage, immunosuppression, photoaging and photocarcinogenesis. FL20 sunlamp, which was employed in this study, emits 25% of its output at UVA wavelengths (Kohmoto, 1996), and UVA irradiance is relatively high in solar irradiation in ordinary life. In the present study, we did not quantify the contribution of UVA wavelengths to photoresponses in XP (-/-) mice. Further studies are currently underway to elucidate the UVA-photoresponses in (-/-) mice.

In conclusion, the present animal experiments suggest that commercially available sunscreen agents for healthy persons can afford protection against increased photoresponses in XP patients. Sunscreens with SPF 10-30 are usually recommended to protect against physiologic sunlight-induced damages (Levy, 1997). However, much higher SPF seems to be necessary to prevent enhanced DNA damage and tumor formation in XP patients. It is needless to say that sunscreens alone cannot provide a perfect protection against severe photosensitivity of XP patients.

Acknowledgments

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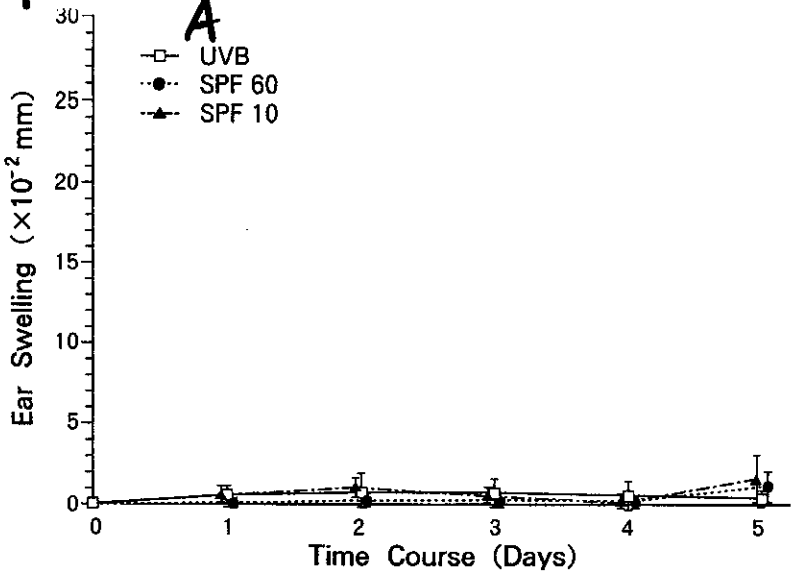
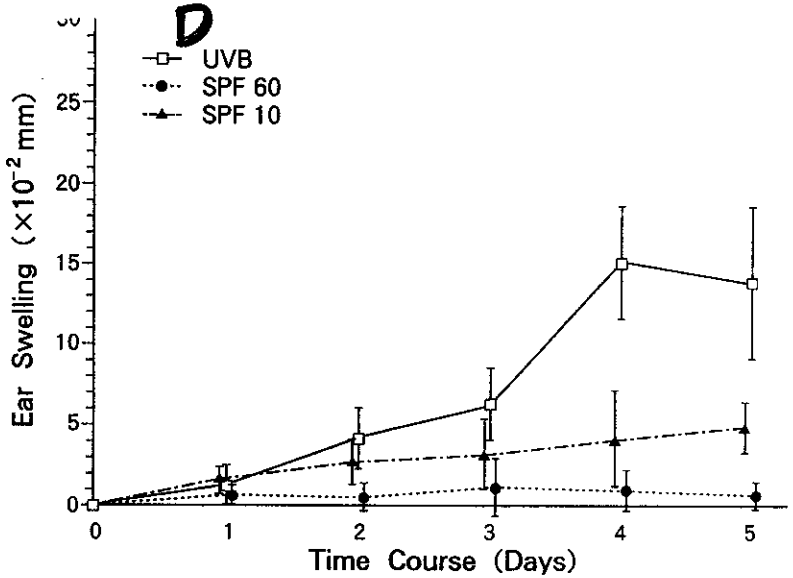
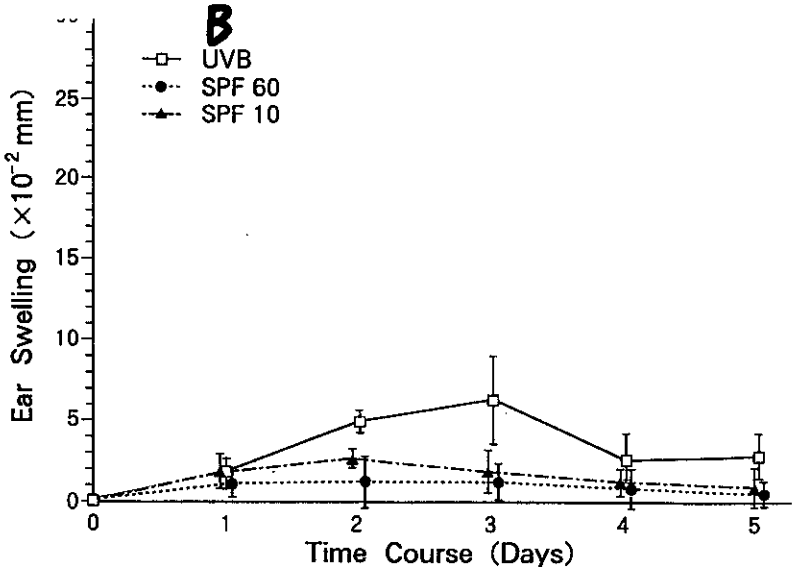
Fig 1


A
UVB
SPF 60
SPF 10
Ear Swelling (×10⁻² mm)
Time Course (Days)


D
UVB
SPF 60
SPF 10
Ear Swelling (×10⁻² mm)
Time Course (Days)


B
UVB
SPF 60
SPF 10
Ear Swelling (×10⁻² mm)
Time Course (Days)

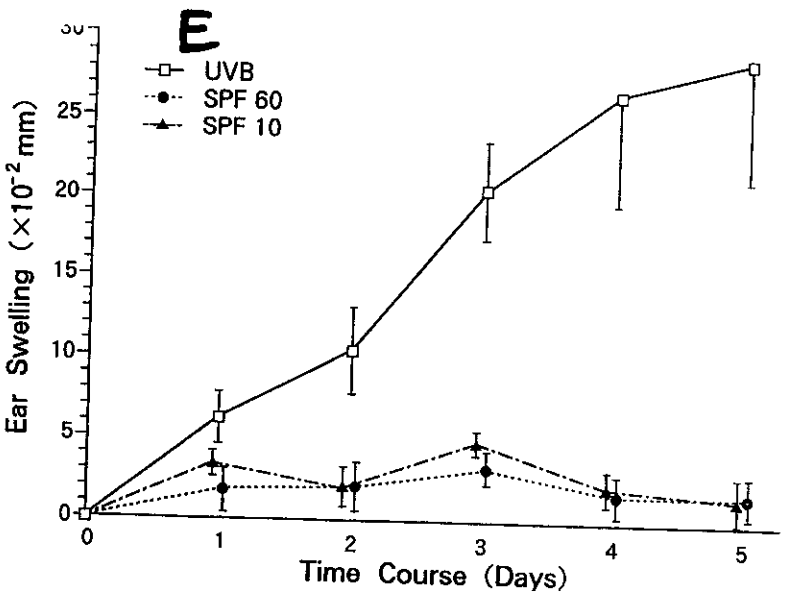
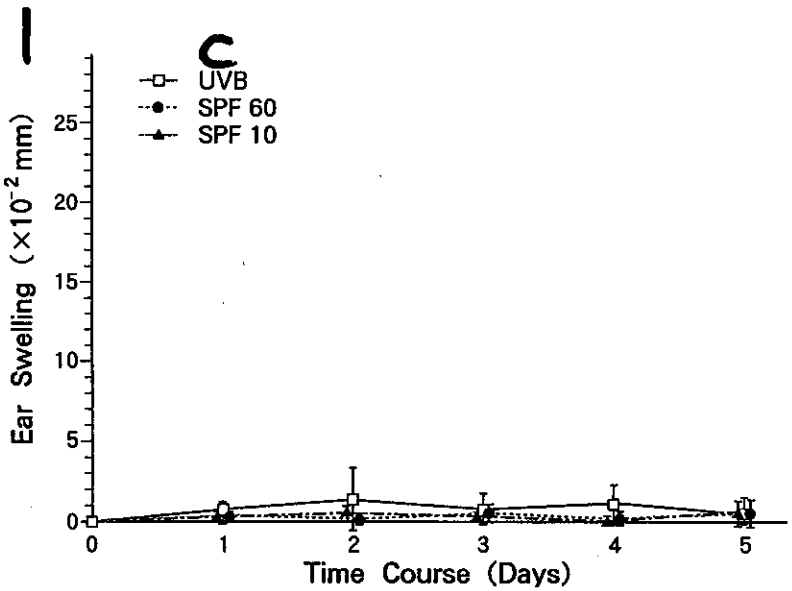

E
UVB
SPF 60
SPF 10
Ear Swelling (×10⁻² mm)
Time Course (Days)

Fig 1


C
UVB
SPF 60
SPF 10
Ear Swelling (×10⁻² mm)
0
5
10
15
20
25
0
1
2
3
4
5
Time Course (Days)

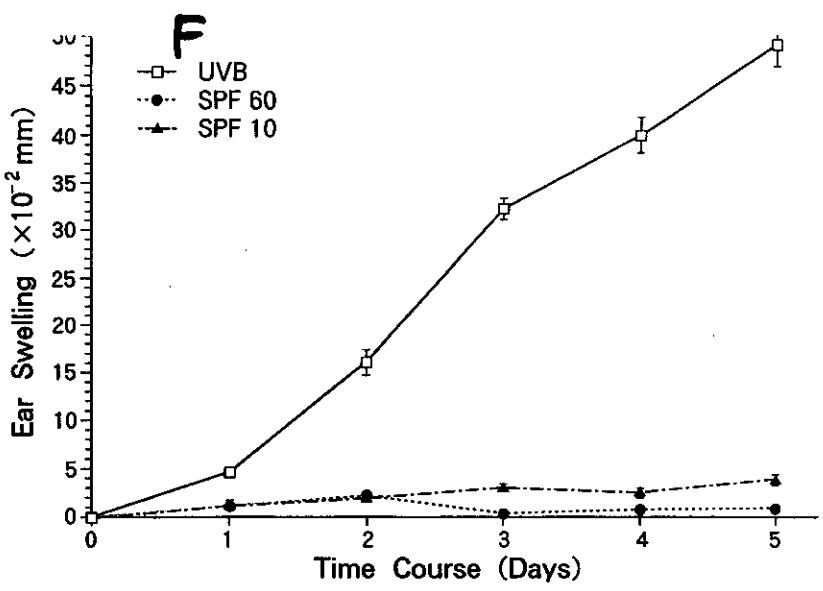
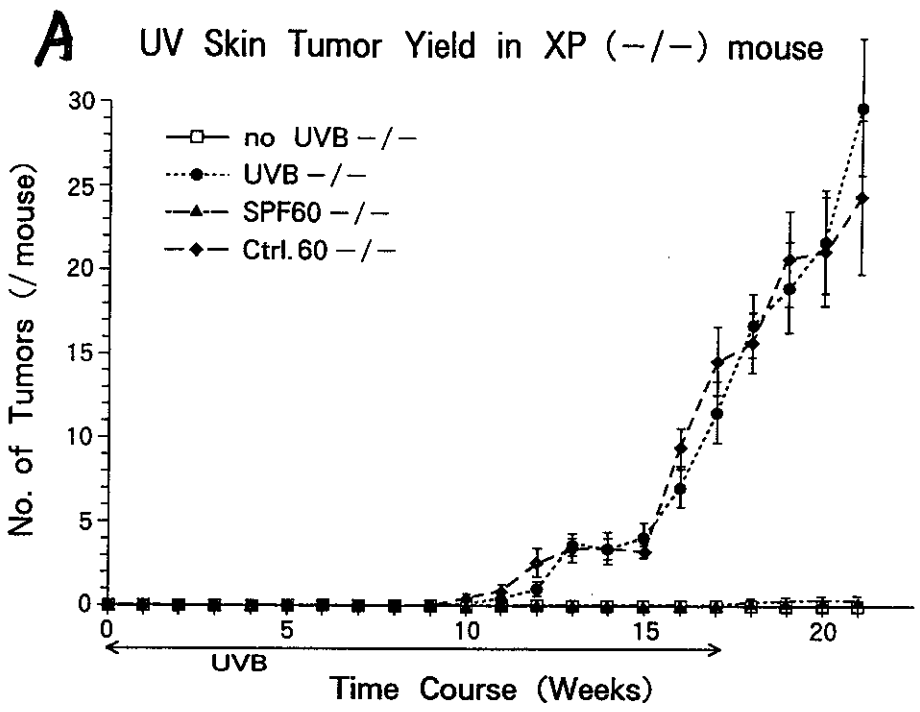

F
UVB
SPF 60
SPF 10
Ear Swelling (×10⁻² mm)
0
5
10
15
20
25
30
35
40
45
0
1
2
3
4
5
Time Course (Days)

Fig 2


A
UV Skin Tumor Yield in XP (−/−) mouse
no UVB −/−
UVB −/−
SPF60 −/−
Ctrl. 60 −/−
No. of Tumors (/mouse)
0
5
10
15
20
25
30
UVB
Time Course (Weeks)

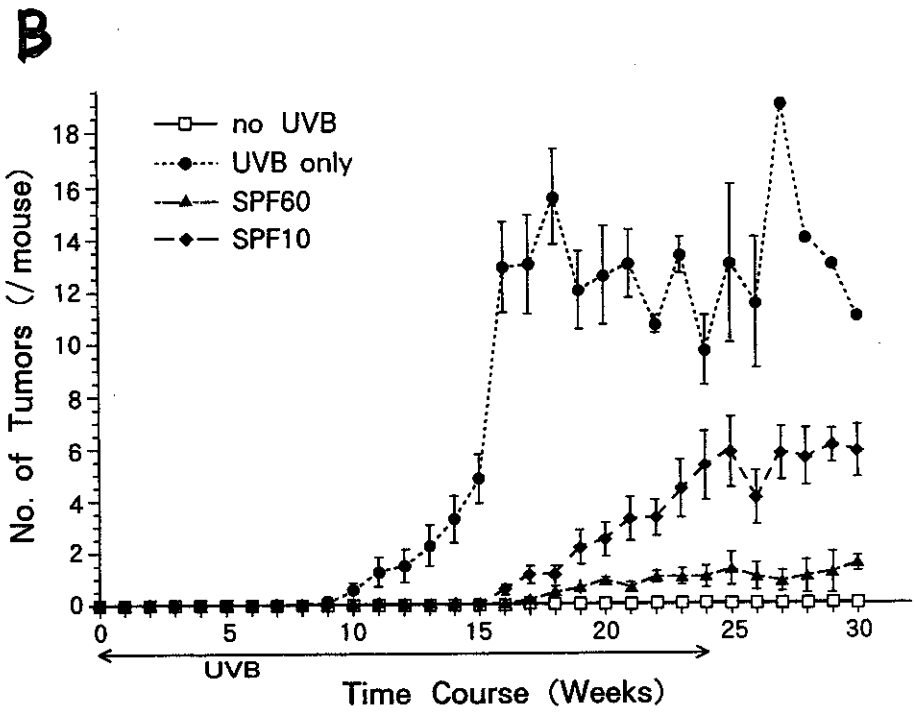

B
no UVB
UVB only
SPF60
SPF10
No. of Tumors (/mouse)
0
2
4
6
8
10
12
14
16
18
0
5
10
15
20
25
30
UVB
Time Course (Weeks)

Table 1

	UVB	SPF 60	SPF 10
>5 mm	2.0±1.15	0	0.13±0.13
>3 mm	4.33±1.76	0	1.13±0.35
all size	13.3±1.29	1.0±0.18	4.38±0.85

number of tumors / mouse ± SD

Table 2

non-UVB	UVB	SPF 60	SPF 10
33.8 ± 6.77	258 ± 35.1	54.3 ± 11.4	372.6 ± 20.9

number of mast cell / mm^2 ± SD

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以降は雑誌/図書等に掲載された論文となりますので、
下記の「研究成果の刊行に関する一覧表」をご参照ください。

「研究成果の刊行に関する一覧表」

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