671 The function of tangerin cells is intrinsically regulated by uracil acid
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Uracil acid (UCA), a byproduct of DNA metabolism, is known to be an important modulator of immune responses of the skin. However, the biological function of this molecule remains largely unknown. In this study, we investigated the role of UCA in regulating the function of Langerin cells (LC). LC are important players in the skin immune system, as their dysfunction is associated with autoimmunity and allergy. Therefore, understanding the function of LC is crucial for the development of new therapeutic strategies. 

In this study, we found that LC isolated from UCA-deficient mice showed impaired antiviral and antimicrobial activities compared to LC isolated from wild-type mice. Moreover, LC isolated from UCA-deficient mice showed reduced expression of pro-inflammatory cytokines, such as interleukin-2 (IL-2) and interleukin-6 (IL-6), in response to stimulation with the yeast-like fungus Pityrosporum ovale. These findings suggest that UCA plays a crucial role in regulating the function of LC and could be a potential target for the development of new therapeutic strategies.

672 The UVA component of solar simulated radiation differentially degrades dermatal proteins associated with photoagging
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Skin exposure to environmental light, particularly UVR, causes a variety of photodamage effects, including premature skin aging (photoaging). This process is characterized by the formation of senescent-like cells, which are associated with a variety of skin diseases. Understanding the molecular mechanisms underlying this process is crucial for the development of new therapeutic strategies.

In this study, we investigated the differential effects of UVA radiation on the expression of key proteins related to photoaging. We found that UVA radiation differentially regulates the expression of a variety of proteins, including elastase, procollagen-1, and fibronectin. These findings suggest that UVA radiation is a key player in the regulation of photoaging-related responses.

673 Galectin-7, induced by cis-urocanic acid and ultraviolet B irradiation, down-modulates cytokine production by T lymphocytes
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Galectin-7 (Gal-7) is a β-galactoside-binding lectin that is expressed by various cell types, including T lymphocytes. Gal-7 has been reported to have a variety of functions, including the modulation of cell-cell interactions and the regulation of cytokine production. In this study, we investigated the role of Gal-7 in the regulation of cytokine production by T lymphocytes.

We found that Gal-7 is induced by cis-urocanic acid (cUCA) and ultraviolet B (UVB) irradiation. Moreover, Gal-7 down-modulated the production of cytokines by T lymphocytes, including interleukin-2 (IL-2) and interleukin-17 (IL-17). These findings suggest that Gal-7 plays a crucial role in regulating the immune response to UVB irradiation.

674 MicroRNA-34a exhibits different responses to ultraviolet radiation and ionising radiation
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MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression by binding to the 3′-untranslated region of their target mRNAs. miRNAs have been implicated in a variety of biological processes, including cell proliferation, differentiation, and death.

In this study, we investigated the differential responses of miRNA-34a to ultraviolet B (UVB) and ionising radiation. We found that miRNA-34a was upregulated in response to UVB irradiation, but not to ionising radiation. Moreover, miRNA-34a was downregulated in response to ionising radiation, but not to UVB irradiation.

These findings suggest that miRNA-34a plays a crucial role in regulating the cellular response to UVB and ionising radiation. Understanding the molecular mechanisms underlying this process is crucial for the development of new therapeutic strategies.
Suppression of UV-induced Wrinkle Formation by Induction of HSP70 Expression in Mice

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2 UVB-induced wrinkle formation due to the degeneration of the ECM is major dermatological problem, in which abnormal activation of MMPs and elastases play important roles. HSP70 has cytoprotective and anti-inflammatory activities. In the present study, we examined the effect of HSP70 expression on UVB-induced wrinkle formation. Heat treatment of the dorsal skin of hairless mice induced the expression of HSP70. The long-term repeated exposure to UVB induced epidermal hyperplasia, decreased skin elasticity, degeneration of ECM and wrinkle formation, which could be suppressed in mice coconcomitantly subjected to heat treatment. The UVB-induced epidermal hyperplasia, decreased skin elasticity and degeneration of ECM were less apparent in transgenic mice expressing HSP70 than in wild-type mice. UV-induced fibroblast cell death, infiltration of inflammatory cells and activation of MMPs and elastase in the skin were also suppressed in the transgenic mice. This study provides the first evidence for an inhibitory effect of HSP70 on UV-induced wrinkle formation. The novel approach to discern the CPD-dependent and -independent effects of UVB and these data will lead to a better understanding of the mechanism of cutaneous defense against sun exposure.

Biological effects of longwave UVA (UVA-1) on human reconstructed skin model

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Freshly cultured human keratinocytes were exposed to UVA (290-320 nm) and longwave UVA (UVA-2, 320-400 nm) and UVA-1, 340-400 nm). UVA-1 which represents the majority of UV wavelengths reaching earth level generates reactive oxygen species and has been shown to induce deleterious effects including immunosuppression and skin cancer, as shown by animal and human in vivo studies. In the present study, the biological impact of UVA-1 was assessed through biochemical and gene expression analysis using a 1D reconstructed skin model including both a fully differentiated epidermis and a dermal equivalent containing human fibroblasts. Forty-eight hours after exposure to 40 mJ/cm2 UVA-1, morphological changes were detected, notably the disappearance of superficial dermal fibroblasts, and a mild alteration of epidermal differentiation. These alterations may be due to a stress-stress related to the exposure of UVA-1. In order to phenotypically characterize the effects induced by UVA-1 on human skin cells, we analyzed the expression of selected genes involved in skin barrier function, down-regulates keratinocyte proliferation and has reduced epidermal expression levels measured in cryosections using quantitative immunofluorescence. In NI skin, CLD-1 expression was significantly reduced in NI skin of PLE patients (p<0.001) compared to controls. This was particularly evident in the stratum spinosum. In healthy skin there was a highly significant reduction (p<0.001) in CLD-1 expression 24 hours after UVA exposure, which was maintained throughout the basal and suprabasal skin layers. In NI skin treated with PLE, CLD-1 expression was significantly reduced (p<0.001) compared to controls. These findings support the hypothesis that overexpression of CLD-1 is beneficial for the prevention of UVB-induced wrinkle formation.

Involvement of MIF in Basal Membrane Damage in Chronically UVB-exposed Skin in Mice

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Solar ultraviolet (UV) exposure is known to induce premature aging of the skin, which is mediated by the matrix metalloproteinase (MMPs) activity. This photodamaged skin is biochemically characterized by a perivascularization of abnormal elastic fibers and a dramatic decrease in dermal collagen. The basement membrane at the dermal-epidermal junction is also damaged during the wrinkle formation process. Macrophage migration inhibitory factor (MIF) is a pluripotent cytokine that plays an essential role in the pathophysiology of allergic inflammation and UV irradiation. In this study, we report that the relationship between the expression of MIF, UVB-induced MMPs activities and skin barrier function is involved in the pathogenesis. The loss of MIF transgenic (TG) and wild-type (WT) mice were exposed to UVB and XUV radiation for 1 week. We found that the back skin of the MIF TG mice had higher MIF, MMP-2 and MMP-9 expression levels than observed in WT mice, and this occurred in a time-dependent manner. Moreover, we observed a decrease in the expression of type IV collagen and increased basement membrane damage in the exposed skin of the MIF TG mice after 1 week of UVB exposure. We therefore concluded that the MIF-mediated enhancement of collagen degradation may contribute to the increased MMP expression in mouse skin following exposure to UV radiation. We next examined the effect of MIF on UVB-exposed mice in keraatinocytes and fibroblast cells of both MIF TG and WT mice. MIF induced an increase in the pro-MMPs expression in keratinocytes and fibroblast cells. However, this increase was not detected in the basal layer of the epidermis. In conclusion, MIF is considered to be an important factor involved in the UVB-induced MMP activity and activation in mouse skin in situ.
683  Differential effects of excimer light (308nm) and narrow-band UVB (311nm) on pigment cell development: Novel insights for better phototherapeutic strategy

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Narrow-band-UVB (NB-UVB) treatment has been widely used for its therapeutic effect on skin as an anti-aging ingredient, retinoids application causes photo-sensitive response such as skin irritation. Thus their daytime usage was not recommended. The aim of this study is to investigate the effects of NB-UVB compared to NB-UVB on mouse skin development. In summary, excimer and NB-UVB lights are both effective for inducing vitiligo repigmentation but via different pathways. The difference in irradiance appeared to play an important role accounting for the more rapid clinical effects observed for excimer light treated vitiligo lesions.

684  UV dose-response and dose-delivery in hairless pigmented mice

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Phototherapy is an important treatment option for vitiligo. Narrow-band-UVB (NB-UVB) has been considered as the treatment of choice. Recently, excimer light (308nm) has been introduced as another option for treating vitiligo. Emitting light at similar wavelength but at much higher irradiance, excimer light has been shown to induce repigmentation of vitiligo more rapidly and efficiently as compared to NB-UVB. Moreover, the lesions that failed NB-UVB therapy also showed response to excimer treatment. Although the wavelength of excimer and NB-UVB light differed by only 5nm to each other, much clinical experience is needed for further clinical effects observed remained obscure. In our in vitro studies, we demonstrated that at similar doses, excimer light imparted different biological effects on primitive pigment cells as compared to its NB-UVB counterpart. Both NB-UVB and excimer light activated intracellular p38 MAPK and p42MAPK signaling pathways involved in the differentiation of primitive pigment cells, although excimer light was more potent than NB-UVB. Excimer light showed significantly higher efficacy in the carboxyfluorescein diacetate-ester (CFDA-ester) uptake assay, which is used to monitor the extent of cell membrane uptake for 30min. Part I showed a linear dose-response curve between log time and log dose. Part II showed that median time to first tumour did not differ between the 4 groups. The medium time to the second tumour was significantly different between 2 SED 2/week and 6 SED 2/week (196 ± 190 days, p<0.001), with no tumours after 4 SED 2/week and 6 SED 2/week (4/183 vs 197 days, p<0.005), but not between the rest of the groups. In conclusion, this study confirms the expected relationship between dose and carcinogenic response. The dose-delivery results showed no difference in time to the first tumor. However, if we include the results for development of the second and third tumour there is a tendency to a more carcinogenic effect at fractionated delivery. This could be due to the fact that mice receiving high exposures develop pigmentation later than mice receiving multiple smaller exposures.
Modulating effect of zinc on cutaneous UVB-response

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Zinc has a large role in the skin’s antioxidant and anti-inflammatory responses. Zinc can enhance the expression of DNA repair genes. We investigated the role of zinc on the cutaneous DNA repair in vitro.

We tested the expression of several genes after treatment with ZnCl2 in HaCaT cells. The results showed that zinc increased the expression of DNA repair genes, including XPC, ERCC2, ERCC3, RER1, and TPOX.

Western blot analysis also confirmed the increase in protein expression of DNA repair genes after treatment with ZnCl2.

Our results suggest that zinc has a protective effect on the skin by enhancing DNA repair pathways.

In vitro photocytotoxicity of a diterpenoid triepoxide on human dermal fibroblasts

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2 Department of Dermatology, Medical University of Vienna, Vienna, Austria

Triptolide, a diterpenoid triepoxide, is a novel anti-photoaging agent. We investigated the photocytotoxicity of triptolide on human dermal fibroblasts.

We exposed human dermal fibroblasts to increasing concentrations of triptolide and assessed cell viability using the MTT assay. The results showed that triptolide induced a dose-dependent decrease in cell viability.

Our findings suggest that triptolide has potential as an anti-photoaging agent for the skin.

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SNEV haploinsufficiency accelerates premature skin aging in response to 8-methoxypsoralen/UV-A treatment in mice

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8-Methoxypsoralen/UV-A (PUVA) treatment is widely used for skin diseases such as psoriasis. The therapeutic effect depends on inducing DNA damage in skin cells. Our study investigated the role of SNEV in the response to 8-MOP/UV-A treatment.

We exposed SNEV deficient (SNEV(-/-)) and wildtype (SNEV(+/+)) mice to 8-MOP/UV-A treatment. The results showed that SNEV(-/-) mice showed increased DNA damage and cell death compared to SNEV(+/+) mice.

Our findings suggest that SNEV has a protective role against DNA damage induced by 8-MOP/UV-A treatment.

Toluidine blue O (TBO) is a dye that stains DNA, and it is used in histological analyses to assess DNA damage. In our study, we used TBO staining to visualize DNA damage in human skin cells exposed to 8-MOP/UV-A treatment.

We exposed human skin cells to 8-MOP/UV-A treatment and stained them with TBO. The results showed increased TBO staining in the 8-MOP/UV-A treated group compared to the control group.

Our findings suggest that TBO staining can be used as a marker for DNA damage induced by 8-MOP/UV-A treatment.
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**Effect of long term PUVA treatment on photoaging in mice with epidermal MnSOD2 deficiency**

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As is known, solar radiation can cause damage to human skin which can physically be observed in cases of photocaging. Substantial research has found that UVA radiation (UV) can be a major contributor to skin aging as well as photocarcinogenesis. However, the UVB radiation that reaches human skin, only 7% is made up of UV in contrast to 54% of infrared radiation (IR). Accordingly, it is known that IR can contribute to skin aging damage. The study aimed to investigate the effects of IR on human skin, yet recent investigations into the effects of UV or IR on human skin are not entirely clear.

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**Tocopherols and tocotrienols (Toco 3.8) reduce proinflammatory interleukin expression of keratinocytes after UVR irradiation**

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Ultraviolet radiation (UV) has profound effects on human skin, causing sunburn, inflammation, cellular injury, cell death, skin cancer and, most of them, are mediated by several keratinocytes isolated keratinocytes. Tocopherols in α, β, γ, δ and tococtrienols (α, β, γ, δ, γ, δ) also named "tocols", are natural compounds found in the Vitamin E complex and their antioxidant behaviour is well-established. Moreover, tocopherols play an important role in skin homeostasis, limiting trans-epidermal permeability of liposoluble substances and regulating keratinocytes turn-over. Recently, it has been demonstrated that tocols are able to reduce gene expression of cyclooxgenase-2 (COX-2), interleukin-6 (IL-6) and MCP-1 of UVB irradiated keratinocytes. In the present study we wanted to investigate whether tocols could be able to modulate the expression of NF-κB and TNF-α in UV-irradiated keratinocytes. Both, UVB dose and suitable tocols concentrations have been selected after multiple cell viability experiments. HaCaT cells were irradiated with UVB (100 mJ/cm²) in the presence or absence of single or mixed tocols and cytokine mRNA levels were examined, by quantitave reverse transcriptase chain reaction, 6 or 24 hours post irradiation, depending on the specific cytokine. The results show that tocopherol alpha and beta dose-dependently down-regulated IL-1β and TNF-α gene expression. Since the regulation of immunomodulatory cytokines is considered an essential part of treatment in multiple inflammatory diseases, tocols may be an interesting option to improve or prevent UV-induced or aggravated clinical conditions.

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**The Effects of Infrared Radiation versus Ultraviolet Radiation in Human Skin Cells**

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We are reporting an ongoing platform to investigate the effects of antioxidants and to elucidate the mechanism of the reported IR induced effects.

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**Systemic photoprotectiveprevention: could a Poly蒲lodium Leucotomos extract enhance the activity of Phyto Dynamic therapy on scalp Actinic keratosis**

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Actinic keratosis is a sun-induced neoplasm that affects the epidermis and which could evolve into squamous cell carcinoma (SCC). Over 80% of the lesions are found in sun-exposed areas such as scalp, face, neck and limbs. Photodynamic therapy PDT is a non-invasive therapeutic method that uses the interaction between visible light and a sensitizing agent (Protoporphirin IX) to generate cell death. PDT is indicated for various dermatological diseases: non melanoma skin cancers (NMSC) and peneplastic keratinocytic lesions. Poly蒲lodium leucotomos (PLE) is a tropical plant part of the Polygonaceae family used in the traditional medicine for inflammatory skin conditions. The active part of the plant, contains phenolic compounds with antioxidants and antiinflammatory and immunomodulatory properties. An extract of the plant is commercially available as oral supplement (Plei). Twelve (12) patients suffering of scalp Actinic keratoses (AKs) were enrolled. The study population was divided into two groups: six (6) received PLE supplementation soon after PDT treatment and six (6) received only PDT treatment. The total count of scalp AKs was recorded before and after (1 and 6 months (T1 and T2) + T0) treatment. The PDT treatment consisted in 2 different sessions (1 week apart) and 0.5% ethosulol-1 acid application and irradiation with a led light 610nm device. At treatments and measurements were performed in winter-time. Both PDT and PLE + PDT treatments resulted in a reduction in AKs count. However, PDT + PLE determined a major decrease in AKs count when compared to PDT treatment alone PLE + PLE = -57.3% at T1, -75% at T2, while PDT alone AKs reduction is -51.5% at T1 and -57.57% at T2. Our preliminary data suggest that Poly蒲lodium Leucotomos Extracts oral supplementation in association with PDT may enhance PDT efficacy in the treatment of AKs by reducing the needs of repeated PDT treatments.

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**Effect of long term PUVA treatment on photosaging in mice with epidermal MnSOD2 deficieny**

As is known, solar radiation can cause damage to human skin which can physically be observed in cases of photocaging. Substantial research has found that UVA radiation (UV) can be a major contributor to skin aging as well as photocarcinogenesis. However, the UVB radiation that reaches human skin, only 7% is made up of UV in contrast to 54% of infrared radiation (IR). Accordingly, it is known that IR can contribute to skin aging damage. The study aimed to investigate the effects of IR on human skin, yet recent investigations into the effects of UV or IR on human skin are not entirely clear.

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**Impact Assessment of Energy Saving Lamps on Photosensitive Skin**

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The purpose of the study was to determine whether energy-saving lamps aggravate photosensitive skin, and to provide evidence based guidelines which help minimize ultra-violet risk. The skin of patients, with a wide range of photosensitive conditions, was exposed to emissions from a single enveloped compact fluorescent lamp, a double enveloped compact fluorescent lamp and a light emitting diode. The lamps were positioned at a worst-case scenario distance of 5cm, using a four aperture minimal erythema dose template. Observation of any erythematic responses was noted immediately, 10, 30, 60 minutes, 24 hours and 248 hours post irradiation. The single enveloped fluorescent lamp induced erythematic responses in 31 out of 195 patients. 10 of these patients, where erythema was induced with the single enveloped lamp, were further tested with a double enveloped compact fluorescent lamp. In 6 of these patients no erythema was induced, the further 4 patients had responses that were reduced in erythematic grading. The light emitting diode did not induce skin erythema in any photosensitive patients. Individuals with Chronic Actinic Dermatitis are the most at-risk patient group from ultra-violet emissions from compact fluorescent lamps. Whilst double enveloped compact fluorescent lamps are a safer alternative for photosensitive individuals, the ultra-violet present may still aggravate other individuals. Light emitting diodes provide a safer alternative energy-saving lamp that reduces the risk of aggravating ultra-violet sensitive skin.

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Beneficial Effect of Coumestrol on Ultraviolet B-Induced Skin Photoaging through Mitochondrial Biogenesis

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Ultraviolet (UV) radiation wavelengths. These first results showed the importance of the design of the investigational model (cells and radiation treatment) to identify new anti-inflammatory compounds.

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UVR induced stress on patients with Porphyria Cutanea Tarda

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Coumestrol is one of phytoestrogens synthesized in response to environmental stress, and commonly found in natural foods such as alfalfa sprouts, clovers, and soybean. In the present study, we investigated the mechanism underlying protective effect of coumestrol on UVR-induced photoaging in human dermal fibroblasts. We found that pretreatment with coumestrol enhanced the UVB-suppressed mitochondrial biogenesis through regulation of Sirt1 expression and activity, and its downstream gene regulation such as PGC-1α, NRF1, and TFAM. Moreover, the ATP and ROS production was restored to normal and the formation of advanced glycation endproducts leading to skin photoaging in skin fibroblasts was blocked by coumestrol pretreatment before UV irradiation. These findings indicate that coumestrol might potentially protect skin photoaging induced by mitochondrial damage and glycated protein production in dermal fibroblasts.