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Skin ageing continues long after ultraviolet radiation damage

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Wrinkling has been attributed to the cumulative effects of acute Ultraviolet Radiation (UVR) exposure on the dermis. Previous studies have shown that the collagenase MMP-1 is secreted by dermal fibroblasts and degrades collagen immediately after UV exposure. However, skin ages gradually, and not intermittently after sun exposure. In this study we sought to examine the mechanism underpinning the gradual appearance of wrinkles, and to determine whether this is a result of intrinsic changes in the biology of the dermis. In vitro studies were performed using patient-derived human dermal fibroblasts from healthy skin, HFF and HDF cell lines. Cell lines were UV-protected or repeatedly exposed to UVB. Dermal fibroblasts from fairer skin types had higher levels of UV-induced mutations which, in multivariate analysis, was linked to higher expression of extracellular matrix degradation genes. This suggests that the background UVR exposure history influences the composition of the dermis as it ages. We investigated the mechanism driving collagen degradation in dermal fibroblasts with and without a history of UV damage. Fibroblasts with high background UV exposure have elevated levels of MMP-1 at rest. In addition, they show increased collagen degradation activity, which persists in the absence of acute UV exposure. Our study shows that dermal fibroblasts with a history of chronic UV exposure have higher levels of collagenase expression and activity, even in the absence of acute UV exposure. Importantly, these findings explain the mechanism driving gradual collagen degradation and wrinkling in the absence of UV light.

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Blue light induced cutaneous signs of photo-aging and protection of the visible effects

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Visible light between 400 to 500nm was identified as an additional contributor to cutaneous photo-aging. Clinical studies showing clear effects of blue light on photo-aging are, however, still scarce. While there is evidence for increased skin pigmentation, the underlying mechanisms of photo-aging in vivo are still not clear. Furthermore, there is still a lack of means to significantly protect from blue light induced signs of photo-aging in vivo. We conducted a randomized, double-blind and placebo controlled clinical study on 33 female Caucasian and Asian volunteers with skin phototype III and IV. We used a repetitive (4x 60J/cm^2, 450 nm) irradiation protocol to induce visible skin pigmentation on inner forearms. We did chromameter measurements to assess skin pigmentation. Using hyperspectral imaging we assessed chromophore status. In addition, we took tape strips which we analyzed for carbonylated proteins. We found significant pigment darkening due to repetitive blue light irradiation (delta ITA° = -16.89, $p<0.001$ vs baseline for the placebo group). Chromophore status showed an increase in melanin after day 4 and temporary increase in hemoglobin and blood oxygen saturation after blue light irradiation. In addition, protein carbonylation increased. Concerning mitigation of the visible signs of blue light induced cutaneous changes, we found that volunteers using a microalgae extract experienced a significantly lower pigment darkening effect compared to the placebo group (delta ITA° = - 11.27, $p<0.05$ vs placebo). We show an efficient and robust protocol to investigate blue light induced cutaneous changes like pigment darkening and signs of photoaging, like protein carbonyls. Furthermore, we propose an extract of the microalga *Scenedesmus rubescens* as an efficient means to protect from visible, blue light induced signs of photoaging.

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Specific Staphylococcal species alter the response of primary human epidermal keratinocyte to ultraviolet radiation

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Skin is the largest organ of the human body and possesses a unique microbiome which is known to play a significant role in skin barrier function. Throughout life, both cutaneous cells and skin microorganisms are exposed to solar ultraviolet radiation (UVR). Although the effects of UVR on keratinocytes have been investigated in many studies, little is known about the effects of UVR on the skin microbiome, and the potential effect of the altered skin microbiome on skin cells. The aims of this study were to test the hypothesis that irradiation of fourspecific skin commensal bacteria (*Staphylococcus epidermidis, Staphylococcus hominis,Staphylococcus capitis* and *Cutibacterium acnes*) change their interactions with normal human epidermal keratinocytes (NHEKs). NHEKs were infected with bacteria and irradiated with solar simulated UVR at different doses. Trypan blue exclusion assay demonstrated that the viability of NHEKs colonized by *S. epidermidis* was 36.3% and 26.1% lower than that of non-infected NHEKs following exposure to 10 and 20 J/cm^2 solar UVR, respectively (n=3). By contrast NHEKs infected by *S. hominis, S. capitis* or *C. acne* showed no significant difference in viability after irradiation. Furthermore, NHEKs exposed to the cell free supernatant of irradiated *S. epidermidis* showed a reduction in viability of 16.7% in response to the 10 J/cm^2 group, and 21.7% to the 20 J/cm^2 group (n=3). However, the viability of NHEKs shown no significant difference in response to the cell free supernatant of irradiated *S. hominis, S. capitis* or *C. acne*. These data suggest that specific members of the skin microbiota may contribute to the deleterious effects to keratinocytes after UVR irradiation.

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A case of acquired dermal melanocytosis associated with Imatinib mesylate treatment

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Imatinib mesylate is a tyrosine kinase inhibitor (TKI) that regulates cell growth, thereby inhibiting cancer cell proliferation. It has been used to treat various neoplasms such as chronic myeloid leukemia (CML). The most common side effect in skin is hypopigmentation. However, hyperpigmentation has also been rarely reported. A 48-year-old woman diagnosed as chronic myeloid leukemia presented with bluish to grayish macules and patches on face, shoulder, and buttock. She had got a treatment of CML with imatinib mesylate for 9 years. She complained hyperpigmentation on face 3 years after the imatinib mesylate treatment. Additionally, the patient reported diffuse bluish to brownish hyperpigmentation similar to Mongolian spot on the upper trunk and buttock appearing about 2 years ago. Histopathologic examination revealed brownish pigmentation of melanin in dermis with dendritic and stellate-shaped dermal melanocytes. In immunohistochemistry, the cells were positive for S-100, Melan-A, and HMB-45. Based on these pathologic findings considering with temporal relationship between the treatment and the clinical manifestations, the diagnosis of an imatinib-induced acquired dermal melanocytosis was made. Imatinib mesylate induces KIT and its ligand stem cell factor (SCF) which inhibits the production of melanin from melanocytes, leading to hypopigmentation. However, some theories postulated it could have different target effects on melanocytes, suggesting melanin production of immature melanocytes could be promoted by imatinib mesylate. In our case, the patient showed hyperpigmentation on typical locations of congenital nevi such as Mongolian spots and nevus of Ito rather than usual locations of the acquired dermal melanocytosis including forehead and zygomatic region. Herein, we report a case of acquired dermal melanocytosis induced by imatinib mesylate, which suggests that immature melanocytes are predominantly distributed in specific areas.

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Negative effect of blue light and potential impacts on the dermis

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Premature skin aging evidenced by a rough skin texture and wrinkles is known to be driven by external factors, mainly by sunlight and in particular UV radiation including UVB (280-320 nm) and UVA (320-400 nm). However, recent advance highlighted the role of visible light and especially the blue light part (400-500nm) in skin aging. As the blue light is the highest energetic wavelength of the visible light, it penetrates deeper into the skin and damages the skin by inducing oxidative stress and production of proteases which degrade the extracellular matrix of the dermis. We first investigated the negative effects of the blue light in human dermis through the evaluation of MMP1 by immunostaining and image analysis on living skin biopsies exposed to blue light irradiation (peak at 250 nm-85 J/cm^2). We further evaluated the blue light preventive effect of a botanical extract selected for its ability to prevent UVB induced oxidative damages by promoting DNA repair system (XPC, DDB2 & POLH) to reduce DNA damages (CPD) and decreasing inflammation (IL1a, PGE2 & LDH). The ingredient was topically applied at 2 mg/cm^2 for 4 days before blue light irradiation. We demonstrated that the blue light significantly increases MMP-1 level by 24%, ($p<0.001$). The plant extract was able to significantly decrease by 43% this MMP-1 induced level ($p<0.001$ versus blue light control) and could protect collagen fibers from the deleterious effect of blue light. As blue light comes from the visible light spectrum of the sun, but its exposure is accentuated by increasing use of artificial sources of light including electronic devices such as cell phone and laptop computers or LEDs from modern habits, it is important to also take into consideration the role of the blue light exposure on skin premature aging to deliver efficient antiaging skin care protection.

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Wavelength characteristics for UVA1 phototherapy with suppressed immediate pigment darkening

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UVA1 phototherapy selectively uses the longer UVA1 wavelengths (340-400 nm), and does not include the shorter UVA2 wavelengths (320-340 nm) or UVB wavelengths (290-320 nm) that cause an erythema reaction. Several studies report the effectiveness of UVA1 phototherapy for various diseases such as atopic dermatitis, T-cell lymphoma, and systemic sclerosis. While UVA1 phototherapy has a high therapeutic effect, it also causes immediate pigment darkening (IPD) as a deleterious effect. IPD is a dull grayish-brown pigment enhancement observed during or immediately after UVA irradiation. IPD begins to disappear 5 to 10 min after irradiation and generally disappears within several hours. Irradiation with UVA at levels several times the threshold level at which IPD develops leads to a persistent pigment darkening that does not disappear even after 24 h and may continue for several weeks. Therefore, IPD may interfere with treatment completion. The peak wavelength of the IPD action spectrum is around 340 nm. In an effort to decrease IPD, we investigated the wavelength characteristics of UVA1 phototherapy. Normal human epidermal melanocytes were irradiated with UVA1 using a short wavelength cut filter or no filter. After irradiation, the cells were incubated for 24 h and tyrosinase mRNA expression was measured by real-time polymerase chain reaction. In addition, the cells were incubated for 8 days and melanin darkening was evaluated by measuring the absorbance of 405 nm using a plate reader. UVA1 irradiation increased the tyrosinase mRNA levels and absorbance — that is, promoted both melanin production and darkening, which was suppressed by use of the filter. These results suggest that the use of a cut filter may suppress IPD during UVA1 phototherapy.