Photoageing – what is it all about?

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Abstract. Photoageing is the addition of chronic UV-induced damage to intrinsic chronological ageing. The three main clinical aspects of photoageing are skin cancers (Figure 1), photoatrophy (Fig. 2) and cosmetic concerns. The mechanisms of photoageing include: activation of skin cell surface receptors by reactive oxygen species (ROS), leading to stimulation of stress-associated mitogen-activated protein; ROS mediated damage to membrane lipids leading to ceramide release and generation of prostacyclins; increased transcription of AP-1 and down regulation of TGF-β, resulting in loss of collagen; induction of various pro-inflammatory cytokines; damage to mitochondrial DNA, leading to reduced ability to generate energy; damage to dermal proteins; and shortening of telomeres, leading to apoptosis and early senescence.

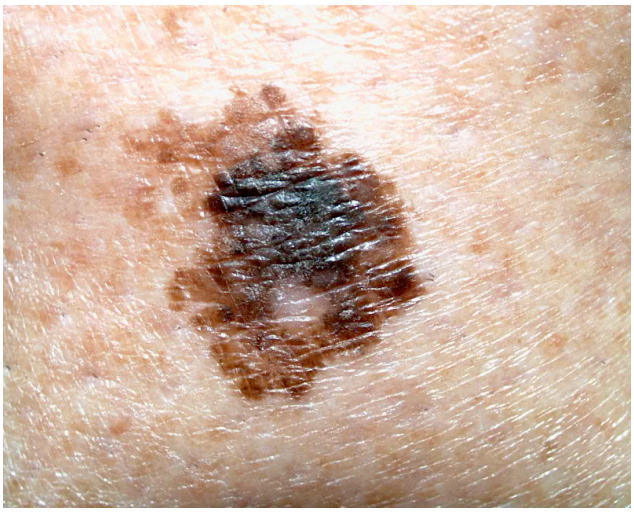

Figure 1. Malignant melanoma.

Mechanism

Within minutes of UV exposure, even as little as 1/10th of an MED (minimal erythema dose), reactive oxygen species are produced in the skin. These can activate skin cell receptors, such as epidermal growth factor (EGF), keratinocyte growth factor, tumour necrosis factor (TNF-α), and interleukin-1 (IL-1). This leads to stimulation of stress-associated mitogen-activated protein (MAP) kinases, which in turn, induce transcription of AP-1. AP-1 interferes with the synthesis of dermal collagen.

In addition, ROS have a direct damaging effect on membrane lipids leading to release of ceramides (reducing the skin barrier function of the skin), which may then be converted into pro-inflammatory prostaglandins.

Furthermore, UV interferes with the signalling of TGF-β, which is needed for both the formation of collagen, and helps prevent keratinocyte proliferation. With the addition of the effect of UV on nuclear factor-kb transcription factor, there is a marked increase in pro-inflammatory cytokines such as IL-1, IL-6, vascular endothelial growth factor (VEGF) and THF-β.

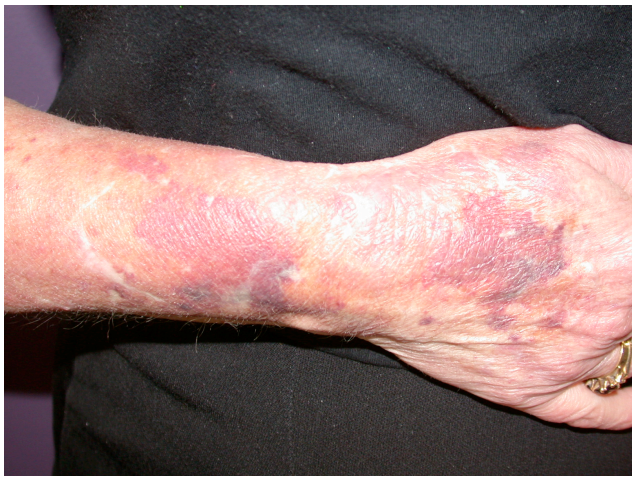

Figure 2. Photoatrophy of the arm.

The above then stimulates the activity of several matrix metalloproteinases (MMPs) and elastases, which degrade collagen and elastic fibres (Fig. 3).

DNA is hypothesized to be the chromophore for the delayed erythema associated with UVB whereas the responsible chromophore for UVA-induced erythema is not known.

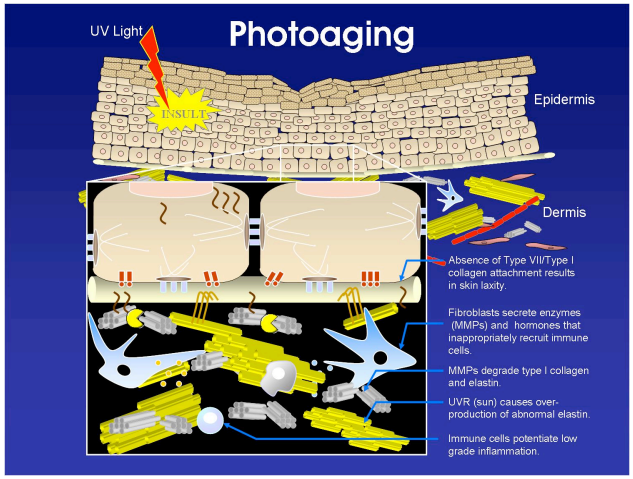

Figure 3. Effect of UV light on collagen metabolism.

UV light induces several different types of DNA damage in a wavelength-dependent manner, such as pyrimidine dimers and oxidative guanine base modifications. Short-term effects of UV include inflammatory infiltrates, vasodilation, formation of sunburn cells, depletion of Langerhans cells, acanthosis and hyperkeratosis. On the molecular level, UV exposure induces stress proteins, and effects both repair processes and cytokine production, such that cells either undergo apoptosis or cease proliferating (cell cycle arrest) in order

to undergo repair. Mitochondial DNA (mDNA) is also damaged by ROS affecting their ability to generate energy.

UVA is a major contributor to protein oxidation in the skin. This leads to inhibition of proteasomal functions and the ability of the cell to successfully degrade additional damaged proteins, particularly in the dermis.

UV radiation (UVR) also affects telomeres. Telomeres cap the terminal portion of chromosomes, preventing their fusion. As chromosomes age, they lose 1-200 terminal base pairs with each cell division. Once the telomere reaches a critical short length, the cell will no longer divide and enters senescence (early cell death).

Prevention and treatment

Sunscreens are the first line of defence against UV irradiation. Smoking accelerates most aspects of UV induced damage. Therefore key elements of prevention of photoageing are sun protection and never smoking.

As photoageing is in part due to UV-induced DNA damage, delivery of enzymes that repair DNA damage may prove to be a useful treatment of photoageing.

The skin contains many antioxidant enzymes (superoxide dismutases, catalases, glutathione peroxidase) as well as non-enzymatic antioxidants (vitamin C and E, Q10, carotenoids), but these become less efficient with age. Various studies have attempted to increase endogenous antioxidant levels with topical and oral antioxidants.

Several studies suggest that low-fat diet confers some protection against the development of actinic keratosis, a UV-induced pre-malignant dysplasia.

Retinoids and alpha-hydroxy acids have been shown to have some beneficial anti-photageing affects (Figure 4).

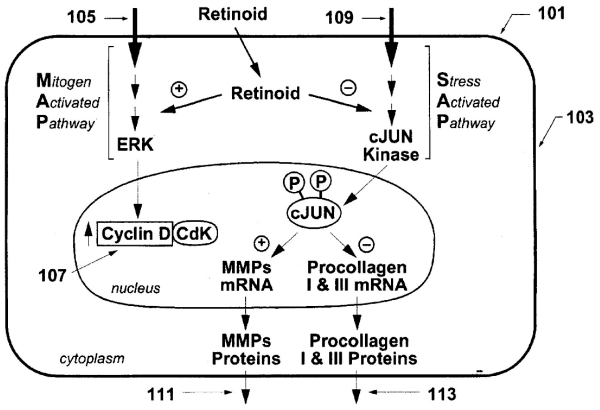

Figure 4. Effect of Retinoids on collagen formation.

Summary

Photoageing is the addition of chronic UV-induced damage on chronological ageing, and accounts for the majority of age-related changes of skin appearance. Understanding the mechanisms involved allows targeting of specific treatments for both prevention and treatment.