IOP Concise Physics

Skin Photoaging

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Chapter 1

Skin aging and photoaging

Skin aging is a complex process resulting in several functional and aesthetic changes. It can be divided into two basic processes: intrinsic or programmed aging and photoaging. Intrinsic aging of the skin, which is characterized primarily by functional alterations rather than gross morphological changes, occurs inevitably as a natural consequence of genetically promoted physiological changes over time (Sanches Silveira and Myaki Pedroso 2014). Photoaging causes premature aging of the skin through cumulative exposure to ultraviolet radiation (UV) from the Sun and artificial UV sources. 'Photo' is derived the Greek 'phos', which means 'light'. The term 'photoaging' was first coined in 1986 to describe the effects of chronic UV light exposure on skin (Kligman and Kligman 1986). The importance of photoaging lies in the enormous number of individuals seeking agents or treatments that can prevent or reverse age-associated changes to the skin. This book mainly reviews the compounds and modalities that have been shown to, or have the potential to, improve the appearance of aged or photoaged skin.

1.1 Clinical features and histological changes

The exact molecular mechanisms of aging and photoaging have not been thoroughly elaborated. The final appearance of aging or photoaging results from a complicated network, including several inflammatory cell-signal pathways, the interactions of many cytokines (IL-1, IL-6, IL-8, GM-CSF, etc) and the self-repairing reaction of damaged cells or tissues. We at least know that the superposition of chronic UV irradiation produces overloaded reactive oxygen species (ROS), which activate cell surface receptors and trigger receptor-initiated signaling, protein oxidation, mitochondrial damage and telomere-based DNA damage responses (figure 1.1). In detail, ROS trigger the release of proinflammatory cytokines and growth factors. Specifically, factors activation protein-1 (AP-1) and nuclear factor-B (NF-kB) up-regulate key matrix metalloproteinases (MMP) such as MMP-1, MMP-3, MMP-8 and MMP-9. Collectively, these proteases degrade the collagen and elastin fibers of

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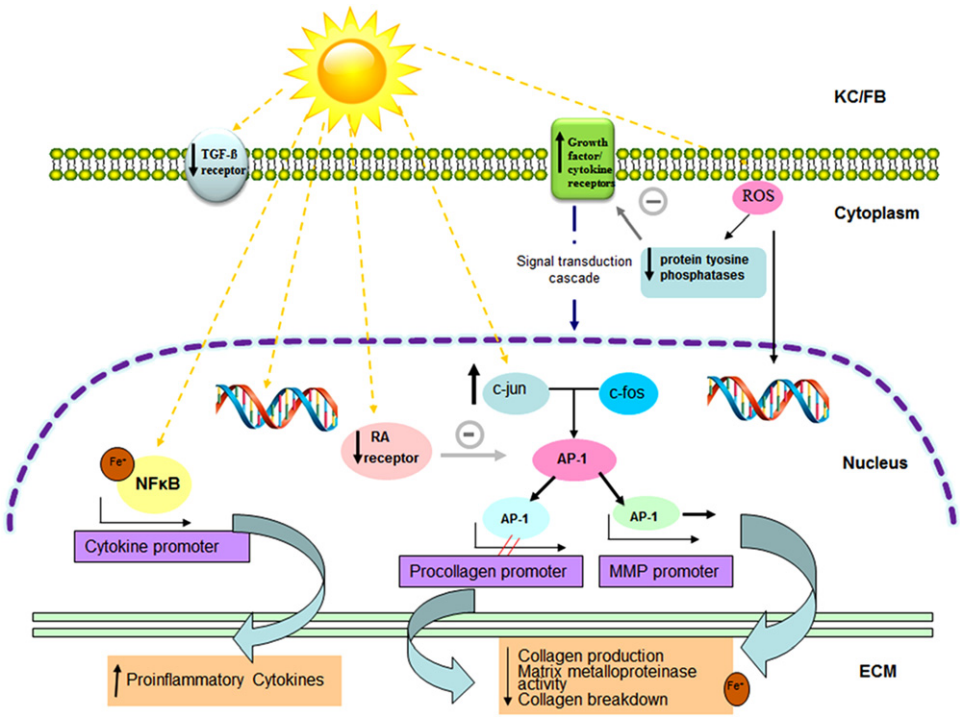

Figure 1.1. Schematic of the pathophysiologic process after sunburn.

the extracellular matrix. What is more, UVR-induced ROS decrease transforming growth factor-β (TGF-β) expression, which decreases collagen production and enhances elastin production. Accordingly, ROS degrade the structural integrity of skin by way of altering the collagen and elastin components of the extracellular matrix. On the other hand, ROS lead to mitochondrial damage and telomere-based DNA damage responses. Many photoproducts of DNA are induced by UVR, including cyclobutane-type pyrimidine dimers, pyrimidine–pyrimidone photoproducts, thymine glycols, cytosine damage, purine damage, DNA strand breaks and DNA–protein cross links. These substances can lead to mutations in the skin cells and ultimately result in aging and even carcinomas of the skin. Many reports have strongly implicated DNA damage or poor DNA repair in intrinsic and extrinsic aging, and this is largely from photoaging (Gilchrest *et al* 2009; Gilchrest 2013; Yaar and Gilchrest 2007). In the face of frequent DNA damage, keratinocytes and fibroblasts might frequently undergo apoptosis or cell senescence (Gilchrest *et al* 2009). In fact, epidermal keratinocytes typically undergo apoptosis more than cell senescence after UV irradiation, leading to what is described as ‘sunburn cells’. Conversely, fibroblasts mainly undergo senescence after either acute DNA damage or multiple rounds of cell division (Gilchrest 2013). Of late, an increasing amount of experimental evidence has pointed towards the telomere-based aging/photoaging mechanism. It has also been well demonstrated that oxidative damage due to aerobic

metabolism or exogenous insults, including UVA irradiation, drives cell senescence through ATM, ATR, p53 and their classic downstream DNA damage signaling pathways (von Zglinicki *et al* 2005). Cell senescence may result from the disruption of the normal telomere loop structure which then initiates telomere-based signaling by similar or identical signaling (van Steensel *et al* 1998; Eller *et al* 2006; Denchi and de Lange 2007; Gilchrest 2013). In summary, these experiments document a crucial role for telomere 'dysfunction' or disruption in initiating DNA damage—such as signaling from telomeres as cells enter replicative senescence (Li *et al* 2004). These observations strongly suggest that intrinsic and extrinsic aging (largely photoaging) may result from activation of the same core mechanism.

The distinction between intrinsic and photoaging of the skin has both clinical and histological significance. These are summarized in table 1.1. Much of the photoaging literature concerns dermal changes, particularly those implicated in wrinkling. Elastosis is the hallmark of photoaging in histopathology, and presents the accumulation of partially degraded elastin fibers in the upper dermis (Gilchrest 2013).

Table 1.1. Typical clinical and histopathological appearance of aging and photoaging.

	Aging		Photoaging
Clinical feature	Skin thinning, laxity and deep, coarse rhytides		Dryness, laxity, dyschromia, telangiectasia, erythema, plaque-like thickening, deep creases and wrinkles, a leathery appearance and cutaneous malignancies (Helfrich *et al* 2008; Gilchrest 1989; Zhang *et al* 2011; Gordon and Brieva 2012)
Histopathological feature	Epidermis	Epidermal atrophy	Epidermal hyperplasia or atrophy
	Dermis	Retraction of rete pegs with flattening of the dermoepidermal interface and dermal atrophy (Kurban and Bhawan 1990)	Disappearance of dermal papillae, thickening of the basement membrane, focally increased numbers and irregular distribution of melanocytes and melanosomes, atypical keratinocytes (Chen *et al* 2009), solar elastosis (Ichinose *et al* 2006), numerous, tangled and hyperplastic fibroblasts, the presence of deformed collagen fibers, decrease in the total amount of collagen and increase to the amount of ground substance (Oikarinen 1990), dilated microvasculature (Schastak *et al* 2008), abundant inflammatory cell infiltration, etc

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