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Abstracts

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The Autophagic System: A New Era in Skin Cell Detoxification

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Cell homeostasis depends on the balance between the biosynthesis and catabolism of macromolecules. There are two major systems in eukaryotic cells that degrade cellular components: proteasome and autophagy. At the basal level, proteasome is involved in degradation of short-lived soluble proteins, while autophagy is a dynamic process that essentially eliminates long-lived proteins (the majority of cellular proteins) and altered organelles such as mitochondria, which are sources of reactive oxygen species and DNA mutations. In the case of more severe stress or moderate but repeated stress, resulting damages can be dramatic for cells. Being numerous, altered intracellular proteins overload and then deplete the degradation capacity of proteasome, and thus accumulate. These modified or aggregated proteins not only become resistant to degradation by the proteasomal pathway but also inhibit the process. Under these conditions autophagy takes over for the proteasome to compensate for its failure. The autophagic machinery ensures the degradation of soluble altered proteins and also maintains its role in elimination of insoluble proteins, oxidized lipids and damaged organelles. Initially described in yeast, the autophagic machinery is now largely studied in neurons, hepatocytes or immune cells since this proteolytic system, or cellular "self-eating", has an astonishing number of connections to human disease and physiology. In skin cells damage due to intrinsic and extrinsic stress seem to be removed by the autophagic pathway, although very few dermocosmetic research studies have been performed. Consequently, the purpose of this article is to analyze the autophagic system in a cutaneous cellular model under conditions of oxidative stress. This new skin cellular system of detoxification may serve as a target for the development of detoxifying active ingredients in cosmetics.

Phase I and Phase II Enzyme Induction in Human Keratinocytes Treated with a Standardized Grapefruit Extract Rich in Bioflavonoids

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Humans are constantly exposed to harmful foreign chemicals and materials from exogenous and endogenous sources. As a result, defense mechanisms have evolved to protect against toxin overload [1] cells are under constant threat from metabolic waste products and xenobiotics. The formation of phase I and phase II metabolism mobilizes and excretes these mainly lipophilic toxins. This clears the cell of molecular rubbish, thereby preventing molecular damage, and aging [2]. According to the literature, citrus fruits rich in bioflavonoids such as naringin and hesperidin [3] can help to protect the body against toxin overload when taken orally [4]. The use of such natural actives is continuously increasing as the understanding of their ability to slow the aging process improves. One of the most powerful detoxification mechanisms is centered on the phase I and phase II enzymes. Phase I activation of lipophilic compounds is carried out by enzymes of the CYP450 family [5]. This phase I biotransformation creates an activated intermediate that is either directly eliminated from the body, or more commonly becomes a substrate for one of the phase II conjugation enzymes prior to elimination from the cell. Phase II enzymes such as quinone reductase perform a broad variety of detoxification reactions. Quinone reductase is able to detoxify a broad range of quinones produced by oxidative metabolism and is known to be expressed in human keratinocytes. Here we summarize two in vitro studies which show that a

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standardized grapefruit extract rich in naringin and hesperidin [3] significantly induces the activity of both phase I and phase II enzymes in human primary epidermal keratinocytes.

Olfaction and Aging

Charles Sell

Olfaction is a very complex sense involving many different steps and involves complicated pattern recognition by the brain. Odorant molecules entering the nose can make contact with both the trigeminal nerves which cover the nasal surfaces, and the olfactory epithelium which is located towards the rear of the roof of the nasal cavity and extending down slightly onto the nasal septum. Seventy percent of odorants stimulate both the trigeminal nerve and the olfactory epithelium. The latter is covered by a layer of mucus and the odorants must cross this aqueous barrier to reach the receptor proteins (ORs) of the olfactory neurons (ORNs). The mucus contains a large variety of chemical species including enzymes which can affect odorants before they reach the receptors. Humans have about 350 active types of olfactory receptor proteins. Each ORN expresses only one type of OR and all ORNs expressing the same OR converge onto a single locus of the olfactory bulb (OB) called a glomerulus. Signals from the OB travel by a variety of routes to the higher brain centres where they are interpreted as odours. The ORs are not odour tuned and the phenomenon of odour is synthesised by pattern recognition of the signals they transmit. However, the ascending signals interact with each other and also with descending signals and signals from other parts of the brain and hence other sensory inputs. Thus visual and taste input as well as experience, expectancy and context all affect the complex signal arising from the OB. Consequently, considerable processing power is required in order to generate the sensation which we know as odour. In view of the number of organs involved, the number of proteins involved and the neural systems required to detect and identify odorant molecules, there is enormous scope for age related deterioration of the body to affect odour perception. Some diseases which are prevalent in the elderly (e.g. Alzheimer's and Parkinson's diseases) are known to have implications for the sufferer's olfactory performance. It is difficult to disentangle statistics on age related smell loss (which inevitably use average figures) in order to determine how much loss is due to disease and how much is an inevitable part of the aging process. There have been many studies on changes in olfactory perception with age. Memory is a key part of odour recognition and age also has a bearing on the emotional and memory effects of odorous stimuli. The literature on these and related subjects will be reviewed.

Blocking Epidermal-Dermal Crosstalk by Strengthening the Intracellular Reactive Oxygen Species Scavenging Capability

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Chronic UV exposure promotes premature aging of the skin which is due to dermal alterations. During this process reactive oxygen species play a pivotal role through induction of the matrix metalloproteinase family. However, although the intracellular effects of reactive oxygen species in keratinocytes and fibroblasts have been recognized, the intercellular effects of reactive oxygen species beyond the basement membrane regarding the induction of matrix metalloproteinases are still unclear. The purpose of this study was to elucidate whether there is crosstalk between keratinocytes and fibroblasts that affects UVB-induced production of matrix metalloproteinase-1 (MMP-1) and to characterize the contribution of reactive oxygen species to that crosstalk. The results show that substance(s) secreted from UVB-irradiated keratinocytes stimulate not only pro-MMP-1 production but also the activation of MMP-1 in fibroblasts. To characterize the contribution of reactive oxygen species to these responses, an effective metallothionein and glutathione inducer, zinc glycine complex (Zn(Gly)2), was used as a tool to reinforce intracellular resistance to reactive oxygen species. Zn(Gly)2 abolished these responses of MMP-1 status, and also suppressed the secretion from UVB-irradiated keratinocytes of tumor necrosis factor-α, interleukin-1α and interleukin-6, which are involved in MMP-1 production. These results demonstrate that reactive oxygen species in UVB-irradiated keratinocytes initiate the production of pro-MMP-1 and its activation in fibroblasts.