

Biochemistry of Skin Aging & Innovative Anti-Aging Strategies

Cilt Yaşlanmasının Biyokimyası ve Yenilikçi Anti-Aging Stratejiler

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ABSTRACT Human skin undergoes an aging process, which is characterized by a loss of elasticity and wrinkle formation. The skin is an important body barrier and is exposed to several different environmental impacts like UV irradiation, dust or ozone, which may influence skin and skin aging. During aging, the products of oxidative processes accumulate and might disturb cellular metabolism. Among them are oxidized proteins and protein aggregates. On the other hand, in a functioning metabolic system oxidized proteins are degraded, mainly by the proteasome. During aging, however, proteasome activity declines. Therefore, the ability to degrade oxidized proteins is attenuated. An age dependent increase in protein oxidation was found in fibroblasts of donors of different ages. Immunohistochemical investigations of the skin showed that in aged skin, an increase of protein carbonyls, one of the most prominent markers of protein oxidation, occurs. It seems during aging, that most of the protein oxidation is accumulated in the dermis. The within the dermis located fibroblasts stay in a quiescent state. This is in clear contrast to the permanently proliferating keratinocytes of the epidermis. Fibroblasts normally do not proliferate, but as opposed to postmitotic cells, they are able to divide again, e.g. during wound healing. We tested in vitro models metabolic changes in fibroblasts during proliferative and non-proliferative senescence.

However, besides intracellular changes in the skin also the extracellular matrix, in particular the collagen fibers are changing. The synthesis and decomposition of such fibers by matrix metallo-proteases (MMPs) are under control of fibroblast metabolism. We assume that the symptoms of skin aging in part are caused by intracellular changes and to another part by an enhanced damage of collagen fibers.

Dermal fibroblasts synthesize procollagen I which is an important component of the extracellular dermal matrix. On the other hand these cells produce MMPs, responsible for collagen degradation, and the (tissue) inhibitors of MMPs (TIMPs). An age-related disrupted collagen metabolism can be, therefore, caused by a decreased collagen synthesis and/or increased collagen degradation. Important transcription factors for the expression of these proteins are AP-1 and NF-kB as they stimulate MMP expression and are concurrently described as ROS sensitive.

UV irradiation, as the most important factor of premature skin aging, also generates a decline of antioxidative defense in skin, as a decrease of superoxide dismutase and glutathione peroxidase activities shown in hairless mice. In parallel, during UV-damage a protein oxidation in human skin takes place. Interestingly, UV decreases the proteasome activity. Recently we were able to demonstrate that protein oxidation in fibroblasts is actively modulating the signal transduction of collagen metabolism proteins.

Most importantly, nutritional influences might modulate the age or UV-damage related changes in skin, but unfortunately not sufficiently enough studies demonstrated such an effect in vivo.

In summary, aging of fibroblasts is characterized by an increase of oxidized proteins and protein aggregates as well as a decreased proteasome activity. The roles of intrinsic and extrinsic factors in these changes in vivo have to be tested further. In conclusion, it might be stated that free radicals and oxidants are certainly important players in skin aging and premature skin aging.

Key Words: Skin aging, oxidative stress, antiaging, collagene, proteasome activity