Aging of Human Sebocytes in vitro Induced by Exposure to a Defined Hormone Environment

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Key Words

Sebaceous gland, aging • Hormones, genes

The skin being a target for a plethora of hormones and also a peripheral endocrine organ by itself [1] can be affected to a large extent by the decline of hormones. For instance, the menopause in females, which is characterized by a sudden decline of sex-specific hormones, is associated with a rapid worsening of skin structure and functions, which can be, at least partially, repaired by hormone replacement therapy or local estrogen treatment [2]. Improvement of epidermal skin moisture, elasticity and skin thickness [3], enhanced production of surface lipids [4], reduction of wrinkle depth, restoration of collagen fibers [5] and increase in the collagen III/I ratio [6] have been reported. However, the role of this multiple hormone lack in the skin aging process remains to be determined. The aim of this study was to evaluate whether circulating hormones in sex- and age-specific levels account for the process of cellular aging and if so which molecular pathways are involved [7]. Human SZ95 sebocytes were treated with a hormone mixture containing growth hormone, insulin-like growth factor 1, 17 β -estra-

diol, dehydroepiandrosterone, testosterone and progesterone in concentrations corresponding to those circulating in young (f20) and postmenopausal women (f60). Expression of the corresponding receptors was identified by RT-PCR and Western blotting, and their cellular localization was detected by immunocytochemistry. Cells incubated with all hormones mentioned above at f60 showed a significantly lower content of sebaceous lipids ($p < 0.001$) compared to cells at f20 relating to in vivo observations, which have documented a decline of epidermal lipids in aged skin [7]. Increased mRNA and protein levels of *c-myc* and increased protein levels of *FN1*, which have been associated with aging in several studies [8–10], were detected in SZ95 sebocytes at f60 compared to those detected at f20 after 5 days of treatment [7]. Expression profiling employing a cDNA microarray composed of 15,529 cDNAs identified 899 genes with altered expression levels at f20 versus f60. Confirmation of gene regulation was performed by real-time RT-PCR. The functional annotation of these genes according to the Gene Ontology identified pathways related to mitochondrial function, oxidative stress, ubiquitin-mediated proteolysis, cell cycle, immune responses, steroid biosynthesis and phospholipid degradation (table 1) – all hallmarks of the aging process [7, 11–17]. This is the first report describing the transcrip-

Table 1. Signaling and metabolic pathways operative in hormonally aged sebocytes (f20 vs. f60) in vitro

Signaling pathways	Number of genes
Steroid biosynthesis	14
C21-steroid hormone metabolism	6
Free fatty acid biosynthesis	7
Free fatty acid metabolism	33
Phospholipid degradation	13
Phosphatidylinositol-signaling pathway	34
Prostaglandin and leukotriene metabolism	14
TGF- β -signaling pathway	44
Complement and coagulation cascade	40
Alzheimer's disease	24
Parkinson's disease	19
Huntington's disease	14
Amyotrophic lateral sclerosis	9
Dentatorubral-pallidoluyasian atrophy	9
Pyruvate metabolism	21

tome of human sebaceous gland cells and its modification by a combination of major hormones in sex- and age-specific levels. Moreover, we provide an in vitro model of endogenous aging which allows a better view into the world of the hormonally affected genes and pathways in human cells. Not only the effects of one hormone as single agent were observed but the effects of a group of hormones in an effort to represent as much as possible the in vivo conditions and to give an insight into the resulting cellular and molecular processes, also altered by interactions of the corresponding hormonal signaling pathways. The identification and molecular characterization of specific genes and pathways affecting hormonal aging is a promising approach, which in the future will certainly provide further clues about the complex network involved in aging. Furthermore, understanding of the underlying mechanisms can be expected to open new strategies to deal with the various age-related diseases.

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