Chapter XIX
The Sebaceous Gland:
A Model of Hormonal Aging

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ABSTRACT

This chapter introduces an in vitro model as a means of studying human hormonal aging. For this purpose, human sebaceous gland cells were maintained under a hormone-substituted environment. This environment consisted of growth factors and sex steroids in concentrations corresponding to those circulating in young and postmenopausal women. The authors suggest that hormone decline, occurring with age, may play a significant role not only in the maintenance of skin homeostasis but also in the initiation of aging. Furthermore, skin, the largest organ of the body, offers an alternative approach to understanding the molecular mechanisms underlining the aging process.

SKIN AGING AND HORMONES

Signs of aging become evident with time, whereas skin provides the first obvious evidence of this process. Since the collection of specimens from internal organs, such as brain, heart, vessels, bones and endocrine glands throughout life for experimental research purposes is associated with major practical and ethical obstacles in humans, interspecies research but also the use of human skin as a common research tool offer promising alternative approaches.

Among multiple factors been involved in the process of skin aging the hormone environment plays a distinct role (Makrantonaki & Zouboulis, 2007). Alterations in appearance due to declining skin quality

are common complaints in postmenopausal women. The postmenopausal skin state is associated with a rapid worsening of skin structure and functions, which can be at least partially repaired by hormone replacement therapy (HRT) or local estrogen treatment (Brincat, 2000). Improvement of epidermal skin moisture, elasticity and skin thickness (Fuchs, Solis, Tapawan, & Paranjpe, 2003), enhanced production of surface lipids (Sator, Schmidt, Sator, Huber, & Honigsmann, 2001), reduction of wrinkle depth, restoration of collagen fibers (Schmidt, Binder, Demschik, Bieglmayer, & Reiner, 1996) and increase of the collagen III/I ratio (Affinito et al., 1999) have been reported. Further potential benefits of long-term HRT are the prevention of osteoporosis and atherosclerotic cardiovascular diseases (Hulley et al., 1998). There has been considerable interest in the possibility that HRT may also be protective against the risk of developing neurodegenerative diseases e.g. Morbus Alzheimer. This remains controversial and the benefit is at present unproven (Yaffe, Sawaya et al., 1988).

Conventional contraindications to HRT include a history of breast cancer or endometrial cancer, recent undiagnosed genital bleeding, active, severe liver disease or a history of thromboembolism. In addition, several current studies, which have shown that the unwished effects are more serious and severe than the advantageous ones have entirely changed the strategy of HRT and limited it in certain cases only (Rossouw et al., 2002; Solomon & Dluhy, 2003)

THE SEBACEOUS GLAND

Sebaceous glands or *holocrine glands* are skin appendages and are found over the entire surface of the body except the palms, soles and dorsum of the feet. They are largest and most concentrated in the face and scalp where they are the sites prone for acne. The normal function of sebaceous glands is to produce and secrete sebum, a group of complex oils including triglycerides and fatty acid breakdown products, wax esters, squalene, cholesterol esters and cholesterol (Downing et al., 1987; Nikkari, Schreibman, & Ahrens, 1974; Ramasastry, Downing, Pochi, & Strauss, 1970; Thody & Shuster, 1989). The most accepted function of sebum is skin lubrication in order to protect it against friction and to make it more impervious to moisture.

Furthermore, sebum lipids transport antioxidants in and on the skin and exhibit a natural light protective activity. They exhibit an innate antibacterial activity and have a pro- and anti-inflammatory function. The sebaceous gland can regulate the activity of xenobiotics and is actively involved in the wound healing process (Zouboulis, 2004). It possesses all enzymes required for the intracellular androgen metabolism and confers upon the skin an independent endocrine function (Fritsch, Orfanos, & Zouboulis, 2001).

With advancing age the size of sebaceous gland cells tends to decrease, while their number remains approximately the same throughout life (Zouboulis & Boschnakow, 2001). Sebaceous gland cells show an age-related reduced secretory output, which results in a decrease in the surface lipid levels and skin xerosis (Engelke, Jensen, Ekanayake-Mudiyanselage, & Proksch, 1997; Pochi, Strauss, & Downing, 1979) - a major characteristic of aged skin. Hormone substitution with estrogens in vivo could significantly reverse skin xerosis indicating a hormone-dependent function of the sebaceous gland cells (Dunn, Damesyn, Moore, Reuben, & Greendale, 1997).

Human SZ95 sebocytes are sebaceous gland cells derived from facial skin and transfected with the SV-40 large T antigen and offer a unique model for investigations on the physiology of aging. They constitute a better alternative to animal research and they functionally behave in a manner concomitant