Editor's Corner

The skin is a fascinating endocrine organ

Jörg Reichrath

Department of Dermatology; The Saarland University Hospital; Homburg, Germany

A few decades ago, the generally accepted views on the function of the skin indicated a more passive role as a barrier against the environment. In the last decades however, it has become clear that the skin represents much more than a passive barrier. This development has been greatly influenced by new insights in the physiological function of the skin as an endocrine tissue. Correlatives for many of the classical endocrine pathways, including parathyroid hormone related peptide-, thyroid hormone-, and vitamin D-pathways have now also been demonstrated in the skin. Consequently, the cutaneous endocrine system is of high importance not only for a broad variety of common skin diseases, such as acne vulgaris, androgenetic alopecia and hirsutism, but also for a multitude of systemic diseases. An example for this relationship is the importance of cutaneous vitamin D synthesis for bone health and reducing risk of chronic deadly diseases including common cancers, autoimmune disorders, infectious diseases and cardiovascular disease. The important role of the skin as a fascinating endocrine, paracrine and autocrine acting organ is highlighted in this issue of *Dermato-Endocrinology*.

In the first paper of this issue, Schneider et al.¹ describe the interaction of nanoparticles with the dermal barrier. This review outlines that the dermal application of drugs via nanoparticles is very promising due to its ease of application and due to the fact that size plays an important role for skin penetration.

In the following paper, William Grant² estimates in his study increases in melanoma and nonmelanoma skin cancer mortality rates and decreases in chronic and infectious disease mortality rates in the United States from the standpoint of approximately doubling population doses of solar UVB to increase mean serum 25-hydroxyvitamin D levels from 16 ng/mL for black Americans and 25 ng/mL for white Americans to 45 ng/mL. He concludes that the primary benefits are expected to come from reductions in cancer and cardiovascular diseases and that, although a few thousand excess deaths per year might occur from melanoma and skin cancer, the avoided premature death rate could be near

400,000/year, with most of the avoided deaths coming late in life. Grant points out that, while oral sources of vitamin D could be used instead of UVB or when UVB irradiance is not available, public health policies do not yet recommend the 3000-4000 IU/day required to raise serum 25-hydroxyvitamin D levels to the levels required for optimal health, which would be required before vitamin D fortification levels in food can be raised. He concludes that until then, moderate solar UVB irradiance remains an important source, and the health benefits greatly outweigh the risks.

The third paper of Grant and Giovannucci³ explain possible roles of solar ultraviolet-B radiation and vitamin D in reducing case-fatality rates from the 1918–19 influenza pandemic in the US. Their findings underline the importance of the cutaneous endocrine system for other organs and adds fatality from influenza to the list of diseases that may be associated with vitamin D-deficiency. This list already includes bone diseases, common cancers, autoimmune disorders, infectious diseases and cardiovascular disease.

The fourth paper of Müller et al.⁴ reports a very interesting clinical case: a recurring mixed-type neurothekeoma of the face.

In the following paper, Grant and Soles⁵ elaborate on the epidemiologic evidence for supporting the role of maternal vitamin D deficiency as a risk factor for the development of infantile autism. As in his previous paper (ref. 3), Grant's findings underline the importance of the cutaneous endocrine system for other organs indicates that infantile autism can be added to the list of diseases that may be associated with maternal vitamin D deficiency.

The next paper represents another very interesting case report by Müller et al.⁶ The authors report clinical, laboratory and histopathological findings in a patient with leukocytoclastic vasculitis associated with acquired reactive perforating collagenosis, representing a diagnostic mimicry.

In the next paper, Sertznig et al.⁷ report their laboratory findings that activation of vitamin D receptor (VDR)- and peroxisome proliferator-activated receptor (PPAR)-signaling pathways through $1,25(\text{OH})_2\text{D}_3$ is of importance for melanoma cell lines and other skin-derived cell lines. They investigated expression of vitamin D receptor (VDR) and peroxisome proliferator-activated receptors (PPAR) α, δ, γ in primary cultured normal melanocytes (NHM), melanoma cell lines (MeWo, SK-Mel-5, SK-Mel-25, SK-Mel-28), a cutaneous squamous cell carcinoma cell line (SCL-1) and an immortalized sebocyte cell

*Correspondence to: Jörg Reichrath; Department of Dermatology; The Saarland University Hospital; 66421 Homburg/Saar, Germany; Email: hajrei@uniklinik-saarland.de

Submitted: 07/24/09; Accepted: 07/24/09

Previously published online as a *Dermato-Endocrinology* E-publication: www.landesbioscience.com/journals/dermatoendocrinology/article/9653

line (SZ95). Interestingly, VDR expression was increased by the treatment with $1,25(\text{OH})_2\text{D}_3$ in $1,25(\text{OH})_2\text{D}_3$ -sensitive melanoma cells but not in $1,25(\text{OH})_2\text{D}_3$ -resistant melanoma cell lines. $1,25(\text{OH})_2\text{D}_3$ increased the expression of PPAR α in almost all cell lines analyzed. These results indicate an important cross-talk between VDR- and PPAR-signaling pathways in various cell types including melanoma cells that may open important new perspectives for treatment and prevention of melanoma and other diseases.

In the following laboratory investigation, Trémezaygues et al.⁸ demonstrate that 1,25-Dihydroxyvitamin D_3 protects human keratinocytes against UV-B-induced damage. The skin is the only organ that has the capacity to photosynthesize the biological active vitamin D metabolite 1,25-dihydroxyvitamin D_3 [$1,25(\text{OH})_2\text{D}_3$] from 7-dehydrocholesterol (7-DHC), following exposure to ultraviolet (UV)-B irradiation. The aim of the present work was to investigate the capacity of $1,25(\text{OH})_2\text{D}_3$ to protect human keratinocytes (HaCaT) and squamous cell carcinoma cell lines (SCL-1) against the hazardous effects of UV-B irradiation. We prove that $1,25(\text{OH})_2\text{D}_3$, in a concentration of 10^{-7}M , protects human keratinocytes (HaCaT) as well as squamous cell carcinoma cell lines (SCL-1) against the hazardous (cytotoxic) effects of UV-B-radiation ($100\text{J}/\text{cm}^2$ - $1000\text{J}/\text{cm}^2$) in vitro. They demonstrate that the number of cyclobutane pyrimidine dimers (CPDs) induced in HaCaT-keratinocytes after irradiation with UV-B ($100\text{J}/\text{cm}^2$ - $1000\text{J}/\text{cm}^2$) was decreased after pretreatment with $1,25(\text{OH})_2\text{D}_3$, as compared to carrier-treated controls. Analysis of the time course revealed that the elimination of UV-B-induced DNA-damage in HaCaT-keratinocytes occurs quicker when cells are pretreated with $1,25(\text{OH})_2\text{D}_3$.

In summary, the original research articles, reviews, and case reports published in this issue underline that *Dermato-Endocrinology* represents a fascinating multidisciplinary and interdisciplinary field. We hope that our journal will continue to be an important forum to spread out *Dermato-Endocrinology* by representing a prominent and exciting venue for relevant research.

References

1. Schneider M, Stracke F, Hansen S, Schaefer UF. Nanoparticles and their interaction with the dermal barrier. *Dermato-Endocrinology* 2009; 197-206.
2. Grant WB. In defense of the sun: An estimate of changes in mortality rates in the United States if mean serum 25-hydroxyvitamin D levels were raised to 45 ng/mL by solar ultraviolet-B irradiance. *Dermato-Endocrinology* 2009; 207-214.
3. Grant WB, Giovannucci E. The possible roles of solar ultraviolet-B radiation and vitamin D in reducing case-fatality rates from the 1918-19 influenza pandemic in the United States. *Dermato-Endocrinology* 2009; 215-9.
4. Müller CSL, Tilgen W, Kutzner H, Pfohler C. Recurring mixed-type neurothekeoma of the face. *Dermato-Endocrinology* 2009; 220-2.
5. Grant WB, Soles CM. Epidemiologic evidence for supporting the role of maternal vitamin D deficiency as a risk factor for the development of infantile autism. *Dermato-Endocrinology* 2009; 223-8.
6. Müller CSL, Tilgen W, Rass K. Leukocytoclastic vasculitis associated with acquired reactive perforating collagenosis: a diagnostic mimicry. *Dermato-Endocrinology* 2009; 229-231.
7. Sertznig P, Seifert M, Tilgen W, Reichrath J. Activation of vitamin D receptor (VDR)- and peroxisome proliferator-activated receptor (PPAR)-signaling pathways through $1,25(\text{OH})_2\text{D}_3$ in melanoma cell lines and other skin-derived cell lines. *Dermato-Endocrinology* 2009; 232-8.
8. Trémezaygues L et al. 1,25-Dihydroxyvitamin D_3 protects human keratinocytes against UV-B-induced damage: in vitro analysis of cell viability/proliferation, DNA-damage and repair. *Dermato-Endocrinology* 2009; 239-245.