In this issue

Prepared by Malcolm B. Hodgins, Mike Edward and David Tillman, Glasgow

Sunscreen Protection Against DNA Photodamage is Related to its SPF

Sunscreen use is advocated to protect against the long-term effects of UVR exposure such as skin cancer and photoageing, and human studies have confirmed their efficacy in reducing the incidence of actinic keratoses and squamous cell carcinoma. There is increasing evidence that nonmelanoma skin cancer involves at least two processes: (i) UVR-induced dipyrimidine DNA lesions, such as cyclobutane pyrimidine dimers (CPD) and consequent mutation of the p53 gene; and (ii) UVR-induced immunosuppression. Although mouse studies have shown that sunscreens can inhibit photodamage, to date there are few quantitative data on their ability to prevent DNA photodamage in human skin *in vivo*. Moreover, no study has assessed the relationship between SPF and the degree of protection from DNA photodamage in human epidermis. In this issue, Young *et al* (p. 37) assessed the ability of two sunscreens, each with an SPF of 4 but with different spectral profiles, to inhibit DNA photodamage in human epidermis. One formulation contained the established UVB filter, octyl methoxycinnamate ($\lambda_{max} = 308$ nm), whilst the other contained terephthalylidene dicamphor sulfonic acid, a new UVA filter ($\lambda_{max} = 345$ nm). Using solar-simulated radiation they showed that exposure to 4 MED with either sunscreen resulted in comparable levels of thymine dimers and 6–4 photoproducts to those produced by 1 MED without sunscreen. This provides evidence that the DNA protection factor is comparable with the SPF and the data support a role for erythema as a good clinical and spectral surrogate for dipyrimidine DNA photolesions in humans. Without dose–response data, however, it was not possible to confirm a specific DNA protection factor. It will be important to determine if there is a comparable protection against mutation. It is also important to stress that epidermal DNA photodamage does occur with suberythemal UV doses. The evidence presented in this paper supports the proper use of sunscreens as one of the means of reducing nonmelanoma skin cancer risk. It is vital, however, that the use of sunscreens is complementary to appropriate sun avoidance behavior, and not viewed as an alternative.

Distinct Actions of Insulin and IGF-1 in Epidermal Keratinocytes

In this issue, Wertheimer *et al* (p. 24) provide new evidence that keratinocytes express both IGF-1 and insulin receptors, but the former seem to relay mitogenic signals while the latter may have a specific role in regulating keratinocyte differentiation. These findings are significant for focusing attention on an old problem: that of how insulin regulates the epidermis. Keratinocyte biologists routinely add insulin to their cell culture medium, and a consensus has arisen that the benefits can be explained largely by insulin's relatively weak affinity for the IGF-1 receptor, which transduces the potent mitogenic effects of IGF-1 in keratinocytes; however, acanthosis nigricans, and other epidermal manifestations of insulin resistance syndromes caused by insulin receptor mutation, lead one to suspect that insulin has a direct role, via its own receptor, in the epidermis. Now Wertheimer *et al* provide evidence that that both insulin receptor and IGF-1 receptor are present on undifferentiated, proliferating mouse epidermal keratinocytes grown in low-calcium, and that total amounts of both receptors do not change appreciably during calcium-induced differentiation. Insulin binding to keratinocytes increased during differentiation, however, while IGF-1 binding decreased, as did ligand-induced autophosphorylation (an index of productive ligand-receptor binding) of IGF-1 receptors. Slightly surprisingly, ligand-induced autophosphorylation of insulin receptors also declined in terminally differentiating keratinocytes, but not to the same extent as for IGF-1 receptors. Finally, insulin enhanced and IGF-1 inhibited the expression of keratins 1 and 10 in cells differentiating in high-calcium medium. Interpretation of these results is somewhat complex, but they do support the concept that insulin and IGF-1 have direct and distinctive roles in the epidermis.

Vascular Endothelial Growth Factor in Chronic Wounds

In this issue, Lauer *et al* (p. 12) have examined the expression of vascular endothelial growth factor (VEGF) and its receptors in chronic leg ulcers. They found that expression of VEGF is elevated, but that the VEGF protein was low compared with the VEGF mRNA signal. It appears that the VEGF may be degraded rapidly, as recombinant VEGF is degraded by chronic wound fluid, while inhibitor studies suggest the involvement of plasmin. Chronic wounds are most commonly associated with chronic venous stasis, diabetes mellitus, and pressure sores that may be particularly debilitating, even leading to limb amputation. Due to their reluctance to heal and tendency to recur, treatment of chronic wounds such as leg ulcers is a major drain on health service resources. Many studies focus upon means of stimulating the healing of chronic wounds, including the use of

0022-202X/00/$15.00 · Copyright © 2000 by The Society for Investigative Dermatology, Inc.

exogenous growth factors, protease inhibitors, and cell engineered dermal equivalents, primarily directed towards providing a matrix suitable for keratinocyte migration and re epithelialization, but few studies actually examine the underlying causes. Chronic wounds are known to contain a number of active proteases, and the rapid degradation of VEGF may well reduce angiogenesis and the formation of granulation tissue. The many proteases present in the wound fluid, however, are also likely to have an adverse effect on matrix proteins involved in facilitating cell migration and angiogenesis. Lauer *et al* have shown that degradation of VEGF could contribute to the poor healing of chronic wounds. The role of VEGF in wound development and recurrence should be explored further.