appear to be structural variants of eumelanins, arising by partial peroxidative cleavage of the 5, 6-dihydroxyindole units [1].

Of the two types of pigments, pheomelanins seem to be less effective than oxymelanins in terms of skin photoprotection, but this is more a matter of surmise than experimental proof. Indeed, we have virtually no data on the photobiological and photochemical properties of isolated native pheomelanins and, especially, of oxymelanins. The difficulties arise from the adverse properties of these pigments which make their isolation and characterisation a most challenging task.

At present, there are no satisfactory tests for distinguishing between pheomelanins and oxymelanins. Pigment colour and solubility in alkali are by no means specific, as well as the ultrastructure of the melanosomes which may be quite similar. It, therefore, seems likely that some of clinical and epidemiological data, relating to pheomelanic phenotypes, might refer in fact to oxymelanic subjects and *vice versa*, which accounts for exisiting confusion regarding skin phototypes, sun exposure and melanoma.

In closing, it can be said that it is a period of renewed inquiry into certain misconceptions and generalisations about melanin skin pigmentation and photoprotection, which have long dominated the field.

WHAT ARE THE DIRECTIONS FOR FUTURE RESEARCH?

1. There is an urgent need to incorporate all the new basic information on melanins and melanogenesis into the current programmes on skin photoprotection and melanoma control.
2. Studies are needed to define more precisely the redox state of the glutathione system in human skin and to evaluate how this relates with the UV susceptibility trait in dark and fair complexioned subjects.
3. A multidisciplinary approach to the development of appropriate technologies for assessment of the amount and type of melanins in human skins of different colour.
4. Pheomelanins versus oxymelanins as risk factors in fair complexioned groups of Anglo-Saxon and Celtic origin.
5. Improved animal models and protocols for studying the putative role of sun exposure in the aetiology of melanoma.

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III. Immunology of UV-Irradiated Skin

J. Krutmann

THE OBSERVATION that ultraviolet (UV) B radiation (290–315 nm) is capable of affecting the skin's immune system gave rise to a novel discipline of biomedical research termed photoimmunology, which investigates the interaction of non-ionising electromagnetic radiation, in particular UVB light, with the immune system [1]. Interest in photoimmunology originated from the observation that UVB radiation is capable of suppressing selected cell-mediated immune responses, including immunity to UVB-induced skin cancer, thereby facilitating the growth of UV-induced skin tumours [2]. There is growing evidence that UVB-induced immunosuppression may be of relevance for the development of both non-melanoma skin tumours (e.g. fibrosarcomas, squamous cell carcinomas) and cutaneous melanomas [3, 4]. The capacity to affect cell-mediated immune responses is not specific for immunity against skin cancer, since UVB light was found to alter the immune response to contact-sensitising agents, to host tissue in graft versus host disease, and to certain microorganisms such as viruses, bacteria, fungi or protozoa [1, 2].

Over the last few years, substantial progress has been made to elucidate the mechanisms responsible for UVB-induced immunosuppression [1]. From these studies it appears that UVB light exerts its immunomodulatory effects not just through one, but rather through an array of interacting mechanisms. Specifically, both direct effects on immunocompetent cells at the irradiation site and indirect effects caused by the release of soluble

mediators, including cytokines, prostaglandins and urocanic acid, apparently contribute to immunosuppression [1]. The most important target cells in UVB-induced immunomodulation appear to be epidermal Langerhans cells and keratinocytes. Much of this knowledge has been generated by studying the UVB-induced alterations in the induction of contact hypersensitivity reactions in animal models. However, an increasing number of investigations, both *in vitro* and *in vivo*, are now performed in the human system as well [5, 6]. Recently, several studies have examined the molecular mechanisms underlying photoimmunological processes. These studies indicate that DNA is the major chromophore in UVB-induced immunomodulation, although other molecules such as urocanic acid may also be of some importance [7, 8]. Further studies to define the exact nature of the DNA lesion relevant for immunosuppression and the signal transducing proteins capable of recognising DNA damage are required in order to fill the gap between the known photobiological events and their immunological consequences. A novel and highly important aspect of photoimmunology is the study of immunogenetics of UV-induced immunomodulation [9]. In this regard it was of great interest to learn that individuals which are susceptible to UVB-induced immunosuppression, as was assessed by their capacity to develop contact hypersensitivity to dinitrochlorobenzene, apparently have a higher risk of developing skin cancer than patients who are relatively resistant to UVB-induced immunosuppression [10]. These studies indicate that susceptibility to UVB-induced immunosuppression may represent a risk factor for the development of skin cancer and emphasise the need for future studies to examine which genetic factors determine the UVB-susceptible status in humans.

It should be noted that wavelengths different from UVB light are also capable of exerting immunomodulatory effects. Accordingly, UVA (320–400 nm) irradiation, in combination with the photosensitising compound 8-methoxypsoralen (PUVA), is currently widely used to treat patients with psoriasis and cutaneous T-cell lymphomas. The fact that PUVA, similar to UVB, is capable of suppressing cell-mediated immune responses may be of relevance to the recent observation that long-term PUVA treatment is associated with an increased risk of developing certain types of skin cancer [11, 12]. Irradiation with high doses of UVA1 light (340–400 nm) is a novel phototherapeutic modality, which may be effectively used to treat patients with acute atopic dermatitis [13]. Although it is currently not known whether high dose UVA1 therapy may affect skin carcinogenesis, there is no doubt that high dose UVA1 irradiation has potent immunomodulatory properties, which clearly differ from those associated with UVB irradiation [13, 14].

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IV. Photoprotection

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MOST RESEARCH and discussion of photoprotection of normal skin has focused on sunscreens which are generally formulated and assessed on their ability to prevent 24-h erythema. Modern sunscreens which contain UVB (280–315 nm) as well as UVA (315–400 nm) chemical filters plus physical UVR scattering pigments such as micronised titanium dioxide are highly effective in this respect. More recently there has been interest in the use of particulate melanins as scattering pigments in sunscreens.

Increasingly, the role of sunscreens in preventing the long-term effects of solar exposure is being discussed and promoted. As such, there is generally a (naive) tendency to assume that because sunscreens afford protection from the acute effects of UVR they will *de facto* afford protection against the long-term effects such as skin cancer and photoageing. Animal data are sometimes cited in support of this assumption. However, such data ignore any effects that sunscreen use might have on behaviour; sunscreen and non-sunscreen treated groups of animals are usually exposed for the same period of time. Animal