UV-induced Melanogenesis Illuminated. Nordic Dermatology Congress, June 2001

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Dr Mina Yaar and Professor Rorsman.

The first plenary lecture at the Nordic Congress of Dermatology in Göteborg, June 2001, held by Dr Mina Yaar of Boston University, was a real high point. Dr Yaar's lecture was a didactic masterpiece. She gave the audience a unique opportunity to follow the important work performed over the last two decades at the Department of Dermatology at Boston University.

Delayed tanning in response to UV irradiation appears within 3-4 days after a single UV exposure. At the same time, an increased tyrosinase activity is observed. The studies made by Yaar and her collaborators have to a large extent been performed on in vitro systems of cultured melanocytes. Such cultures have been extensively investigated by the Boston group since the findings of Eisinger and Marko in 1982, who reported on the importance of certain growth factors for the stimulation and differentiation of normal melanocytes. It had previously only been possible to cultivate malignant melanocytes, but from 1982 on, it became possible to study the physiology, biochemistry and pharmacology of "normal" melanocytes.

UV, both UVB and UVA, are potent stimuli of melanogenesis. UV photons interact with many molecules in the skin, and products of such interactions have been studied for their activity as mediators of increased melanogenesis. Irradiation of cell membranes leads to liberation of arachidonic acid. This compound is metabolized to various prostaglandins and leukotrienes which all may participate as stimulators of melanin formation.

UV also generates DNA damage, leading to photoproducts formed at dipyrimidine sites; the most abundant ones are cyclobutane pyrimidine dimers. UVB appears to act directly on the nucleotides, while UVA needs the presence of oxygen, which may indicate a free radical involvement in the UVA response.

Yaar and collaborators have found that thymidine dimers can induce increased thyrosinase activity and increased melanogenesis. In contrast, deoxyadenine dinucleotide, a dinucleotide rarely involved in photoproduct formation, had no effect on melanogenesis. The effect of the thymidine dinucleotides was mediated at least in part through induction of p53.

The thymidine dimer was active when applied topically to guinea pig skin and the induced tanning was protective against UV irradiation.

A large number of single-stranded DNA fragments were examined for melanogenic activity. Effective sequences were noted to have homology to telomers, the terminal portions of eukaryotic

chromosomes that consist of tandem repeats of TTAGGG. Therefore an 11-base nucleotide homologous to the telomer was tested for induction of melanogenesis. The thymidine dimer increased melanin 3-fold above control, but the telomere homologue increased melanin by 10-fold. This effect, too, was mediated by p53.

In the discussion Dr Yaar suggested that the melanogenic effects of UVA may be mediated by other nucleotide sequences, since guanine dinucleotides are the main products of UVA-induced DNA damage.

It will be most interesting to learn of a possible increase of tyrosinase-related protein 1 (TRP 1) after melanin stimulation by telomerase nucleotides, since TRP 1 is strongly linked to eumelanogenesis.

The levels of melanocyte-stimulating hormone (MSH) and proopiomelanocortin (POMC) in the skin are increased by UV irradiation. The melanocortin I receptor (MCIR) on the melanocytes is also influenced by UV. It seems possible that telomeric oligonucleotides, too, mediate these responses.

Dr Yaar's lecture fascinated us all and evoked the greatest respect and admiration for her research group and for Bostonian basic science in dermatology.