

LETTER TO THE EDITOR

Photobinding of 8-Methoxypsoralen at Psoriasis Skin

Sir,

Seven years after the worldwide introduction of photochemotherapy (PUVA therapy) using 8-methoxypsoralen (8-MOP) and longwave ultraviolet light, its mechanism of action remains unclear. Whether 8-MOP passes to the human epidermal cell nuclei and reacts there with nucleic acids, or whether it becomes trapped by membranes or other cell constituents on its way, has not been demonstrated up to the present. Because of possible late effects such as cancerogenesis, this question is of great practical importance.

Recently Dr Bertaux and co-workers (1) investigated the binding of 8-MOP under PUVA-like conditions in psoriatic skin *in vitro*. By using an autoradiographic technique, they found an equal amount of photobinding in both nucleus and cytoplasm. However, in contrast to other topics investigated, the authors did not report any quantitative data regarding the silver grains inside the nuclei versus those outside.

In analysing the data and figures published, we would like to make some comments. This autoradiographic technique, including incubation procedures and preparation of 1 μm sections, is a very sophisticated one. In the upper part of Fig. 1 one can see some silver grains outside the section. Thus a greater or lesser degree of dislocation of silver grains would seem possible.

Answer

Sir,

In response to the stimulating comments of H. Meffert and N. Sönnichsen we want to underline some points.

In our experience, autoradiography of 1- μm epoxy sections from a large surface area is a quick, reliable and convenient technique giving quite different but complementary information, as com-

Regarding the living epidermal cell layers, the distribution of silver grains in Fig. 1 can be interpreted primarily as revealing a preference for the intercellular spaces. Secondly, the linear arrangement of silver grains close the nuclear membrane is conspicuous. Previous investigations showed firm binding of 8-MOP to cell membranes and to cytoplasmic constituents following UVA irradiation of human skin *in vivo* (2). Interestingly, *in vivo* 8-MOP could not be confirmed inside the cell nuclei.

Summing up both the papers cited, there is so far no firm evidence of photobinding of 8-MOP to epidermal nucleic substrates in living human cells.

REFERENCES

1. Bertaux, B., Dubertret, L. & Moreno, G.: Autoradiographic localization of 8-methoxypsoralen in psoriasis skin *in vitro*. *Acta Dermatovener (Stockholm)* 61: 481, 1981.
2. Meffert, H., Barthelmes, H., Metz, D. & Sönnichsen, N.: Fotochemotherapie mit 8-Methoxypsoralen und UVA. III. Fluoreszenzmikroskopische Untersuchung der Bindung und des Transportes von 8-MOP in der menschlichen Haut. *Dermatol Monatsschr* 163: 619, 1977.

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pared with fluorescent techniques performed on unfixed tissues. Our techniques visualize only covalent photobinding between 8-MOP and tissular targets not extractable by the embedding procedure.

Fluorescence is not very sensitive for the study of 8-MOP as a result of the relatively weak fluorescence of this drug. Moreover the fluorescence of psoralen disappears after covalent binding with a cellular target, thus explaining the negative results of the authors (1). However, fluorescence is

a very convenient technique for the study of mild lesions of 8-MOP in extractable targets of possible therapeutic importance such as membranes. Thus these two techniques give complementary results.

We would like to respond briefly to other comments. Silver grains from the upper part of the section presented in Fig. 1 are linked with keratin scales which strongly bind 8-MOP after UVA irradiation. In all our studied sections no peculiar relationship between covalent linkage of 8-MOP and cellular membrane was noted. The ratio between silver grains inside the nucleus and in the cytoplasm has been calculated. On one hundred cells: 40% of the silver grains were observed in the nucleus and 60% in the cytoplasm in the stratum spinosum of normal skin; 20% of the silver grains were observed in the nucleus and 80% in the cytoplasm in the stratum spinosum of psoriatic skin. This discrepancy is explained by the increase in the cytoplasmic volume of keratinocytes in psoriatic stratum spinosum. The density of silver grains per

area unit is the same in normal as in psoriatic epidermis.

In conclusion, firm evidence of photobinding of 8-MOP in the nucleus of living human keratinocytes has been adduced in confirmation of previous results.

REFERENCE

1. Dall'Acqua, F., Vedaldi, D., Bordin, F. & Rodighiero, G.: *J Invest Dermatol* 73: 191-197, 1979.

Received April 7, 1982

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ANNOUNCEMENTS

Pediatric Dermatology Seminar X—Final notice. The 10th Pediatric Dermatology Seminar will convene at the new Carillon Beach Hotel, Miami Beach, Florida, February 24-27, 1983. Guest Speakers will include: Yehudi Felman, Arthur Norins, Heinz Eichenwald, Arthur Rhodes, Guinter Kahn, Mark Dahl, Lawrence Schachner, etc. The seminar fee is \$240.

A seventeen day post-seminar tour to China will visit Kweilin, Hangchow, Peking, Wuxi, Shanghai, Suzhou, and Hong Kong. (All inclusive costs \$2 395.) CME credit is given.

For information contact: Guinter Kahn, M.D., 16800 N.W. 2 Ave. no. 401, Miami, Florida 33169, USA.

International Conference on Psoriasis Care. August 28-31, 1983, Gothenburg, Sweden. The University of Gothenburg and the International Federation of Psoriasis Associations are organizing a conference to present the scientific basis for psoriasis

care and gather clinical experience from leading dermatologists in the world. Other topics are the problem of organisation of psoriasis care, different conditions for psoriasis care in different parts of the world and consequences for the quality of life for the patients.

For information contact: PSO-CARE, Dpt. of Dermatology, University of Gothenburg, Sahlgren's Hospital, S-413 45 Gothenburg, Sweden.

The 10th Annual Meeting of the Society for Cutaneous Ultrastructure Research (SCUR) and The 4th International Dermato-pathology Colloquium of the International Society of Dermato-pathology will be jointly held in Berlin (West), on June 15-18th, 1983. Chairman: Prof. Dr. C. E. Orfanos.

For further information contact the secretary Dr. D. Tsambaos, Department of Dermatology, University Medical Center Steglitz, Hindenburgdamm 30, D-1000 Berlin 45, West Germany.