Keratin 17: a useful marker in anti-psoriatic therapies

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The investigation of changes that take place during development or therapeutic regression of psoriatic lesions can give us a clearer insight into processes that are of importance in the pathogenesis and treatment of this disease.

In previous studies, different parameters have been used to investigate increased epidermal cell proliferation and disturbed differentiation in psoriasis. The histological appearance [6, 10, 11], percentage of cells in SG2-M-phase [1], incorporation of ³H-thymidine [2], or BrdUrd [13], Ki-67-staining [3, 13], and up- or down-regulation of distinct keratins [7] have been used as parameters.

The aim of the present study was to investigate further the effect of anti-psoriatic therapies on keratin expression in human epidermis. In psoriasis, keratins are expressed that are only found in small amounts or not at all in normal human skin. Also down-regulation of keratins that are related to differentiation takes place [14].

Assessing the amount of keratin numbers 2, 10, 16 and 18 in psoriatic skin has proved to be a useful approach in monitoring therapies. Keratin 16, especially, correlates well with progression or regression of the lesions [4, 7].

Keratin 17 is not present in normal human epidermis; it is restricted to the lower part of the outer root sheath of the hair follicle, and to myoepithelial cells of the sebaceous gland. It is expressed by basal cell carcinomas, which has led to the hypothesis that basal cell carcinomas have a follicular origin [8, 12]. A correlation of keratin 17 expression and hyperproliferation has also previously been suggested [8, 12]. Recently the expression of keratin 17 has been shown in lesional psoriatic epidermis of the scalp [16].

In this study the presence and localization of keratin 17 in psoriatic lesions was investigated further and the effect of anti-psoriatic therapies on keratin 17 expression in such lesions was studied using monoclonal antibody E3 on frozen sections.

Six patients suffering from psoriasis participated in this study. They had not received topical treatment for at least 2 weeks, or systemic treatment for at least 2 months. Three patients were treated with anthralin in a cream base and three patients were treated with the new vitamin D₃-analogue MC903. Clinical response was measured using the PASI score. Biopsies from psoriatic lesions were taken before therapy and after 8 weeks of anthralin treatment or after 12 weeks of MC903 treatment. The biopsies were snap-frozen in liquid nitrogen, and stored at −80°C. Frozen sections (7 µm) were cut and fixed in acetone (4°C, 10 min). Staining with the mouse monoclonal antibody E3 to keratin 17 [12] was performed using a dilution of 1:10 in phosphate buffered saline (PBS). Incubation for 30 min at room temperature in the dark was followed by 3 washes with PBS. The sections were then incubated for 30 min with a peroxidase-conjugated rabbit anti-mouse antibody (Dakopatts, Copenhagen, Denmark) diluted 1:50 in PBS containing 5% human AB serum. After three more washes in PBS and preincubation with sodium acetate buffer (pH 4.9), E3 binding was visualized in sodium acetate buffer containing 200 µg/ml 3-amino-ethyl-carbazole (AEC) and 80 µl/l H₂O₂. Finally slides were counterstained with Mayer's haematoxylin and mounted in Kaisers glycerin gelatin.

Results of the staining reactions with the antibody E3 in untreated psoriatic skin and in anthralin- or MC903-treated psoriasis are shown in Table 1. Staining with the keratin 17 antibody showed a consistent pattern in all biopsies of untreated psoriatic skin. Keratin 17 was present in the upper layers of the suprabasal compartment and was evenly distributed over the total length of the sections (Fig. 1A). Post-treatment biopsies showed a clear reduction in keratin 17 (Fig. 1B). In four out of six patients no keratin 17 expression could be found at all after treatment (three patients treated with anthralin, one patient treated with MC903). In one only sporadic keratin 17-positive cells were present after therapy, while the
remaining patient still showed considerable staining for keratin 17 in the post-treatment biopsy. This patient also showed the smallest reduction in PASI score. The presence of keratin 17 was most pronounced in areas that showed distinct hyperparakeratosis. No keratin 17 expression was seen in the basal layers of the epidermis.

All patients showed a marked improvement in their psoriatic lesions during the treatment period. The average reduction in PASI score was 8.2, varying from 2.4 to 19 (Table 1).

Keratin expression in different epithelia has been extensively investigated during the last decade. Various types of epithelia show different patterns of keratin expression. In addition, many tumours and cultured cell lines partly retain the keratin composition and distribution of their tissue of origin [9].

In all biopsies of untreated psoriatic lesions, E3 staining was observed in the most superficial layers of the living epidermis, just beneath the stratum corneum. Keratin 17 is not present in normal interfollicular epidermis, and in other epithelia exclusive staining of the basal cell compartments has been reported [12]. The results of the present investigation suggest an association with abnormal terminal differentiation more than with hyperproliferation of keratinocytes in psoriasis, since keratin 17 is seen exclusively in the upper layers of the stratum spinosum.

Based on immunohistochemical studies using the antibody Ks8.12, keratin 16 was found to be present not only in the most superficial layers of psoriatic lesions, but also in the entire suprabasal compartment. Keratin 16 is a well established marker for hyperproliferation of keratinocytes [15]. During treatment with anthralin and with MC903 the expression of keratin 16 is reduced [3–5]. Treatment with anthralin or MC903 resulted in an even more marked decrease in keratin 17 expression, which correlated well with the clinical response.

References

1. Bauer FW, Crombag NHCMN, de Grood RM, Boezenman JB (1980) Quantification of deviations of the epidermal DNA-


5. Mare S de, Jong EMGJ de, Erp PEJ van, Kerkhof PCM van de (1990) DNA content and Ks8.12 binding of the psoriatic lesion during treatment with the vitamin D₃ analogue MC903 and betamethasone. Br J Dermatol 11:291–295


