Sequence of Changes in Psoriatic Epidermis*

Immunocompetent Cell Redistribution Precedes Altered Expression of Keratinocyte Differentiation Markers

WALDEMAR PLACEK,[1,**] MAREK HAFTEK[2] and JEAN THIVOLET[2]

[1]*Department of Dermatology, Medical Academy of Gdansk, Gdansk, Poland, and*
[2]*Laboratoire de Recherche Dermatologique et Immunologie CNRS UA 601, Clinique de Dermatologie, PavR, Hôpital Edouard Herriot, Lyon, France*

Placek W, Haftek M, Thivolet J. Sequence of changes in psoriatic epidermis: immunocompetent cell redistribution precedes altered expression of keratinocyte differentiation markers. Acta Derm Venereol (Stockh) 1988; 68: 369–377.

Recent studies suggest that the immune system is involved in the pathogenesis of psoriasis. We studied the expression and distribution of immunocompetent cells and of some chosen differentiation antigens of keratinocytes at various stages of lesion development, using indirect and amplified immunofluorescence, and avidin–biotin–peroxidase method. Serial cryostat sections were collected so as to allow comparative studies of adjacent parts of each biopsy sample with various immunocytochemical markers. Our results indicate that focal intra-epidermal infiltration of otherwise unaltered epidermis with lymphocytes, mostly of the T-helper phenotype, was the first perceptible change occurring in patients with eruptive psoriasis. Modification of the Langerhans' cell staining was observed in these initial subclinical lesions. A significant reduction of the cell frequency was noted in psoriatic papules and plaques. Changes in the epidermal antigen expression could be observed in the developed lesions only. The simultaneous appearance of histologic signs of psoriasis and the modification of keratinocyte antigens indicates that both events are related to the epidermis hyperproliferation, possibly induced by focal inflammatory reaction. (Received December 7, 1987.)

M. Haftek, Pav. R, Clinique de Dermatologie, Hôp. E. Herriot, 69437 Lyon, France.

Several recent reports point to an immunological mechanism in pathogenesis of psoriasis. According to some authors (1–6), T-lymphocytes play the main role in this process. Polymorphonuclear leukocytes in the earliest stages of clinically incipient psoriasis have also been observed and considered as a possible primary pathogenetic factor (7, 8). Changes in Langerhans' cell (LC) distribution in well developed psoriatic lesions have been reported (2, 9–13). The LC population is influenced by successful anti-psoriatic treatments (11–15). A possible central role of LC in the initiation of new psoriatic lesions has been postulated (15, 16).

We have performed morphological and quantitative studies on dendritic T6 and HLA-DR positive cells and quantitatively examined subsets of T lymphocytes in the epidermal infiltrate at various stages of formation of psoriatic lesions. We also attempted an examination of the sequence of events occurring during the formation of new psoriatic lesions, comparing clinical picture, histology and expression of various epidermal differentiation antigens with the results of our study on immunocompetent cells.

MATERIALS AND METHODS

Patients and biopsies

Thirty-two skin biopsies from 9 patients (7 men and 2 women, aged 16–80 years) with untreated psoriasis and three biopsies from 3 healthy controls were studied. Two patients had non-active plaque psoriasis (A0), 2 had peripherally spreading lesions (A1), and 5 displayed a very active form of illness, forming

*Presented in part at the Congrès Annuel de la Recherche Dermatologique, October 16-18, 1987, Bordeaux, France.

**Dr W.Placek, Fellow, with a Polish–French scientific exchange scholarship.

numerous new papules (A2). Some of the A2 patients had also peripherally growing plaques. In all cases, punch biopsy or lancet biopsy specimens of the skin were taken from the lower back. Twelve biopsies were taken from non-involved psoriatic skin (NIPS), 11 from well-developed psoriatic lesions (DPL), and 9 from pin-point (PP) lesions. The biopsies were snap-frozen in liquid nitrogen, embedded in Tissue-Tec (Reichert-Jung, W. Germany) and cut into 4-μm frozen sections in a manner permitting parallel examination of the adjacent sections with various immunohistochemical markers. The numbered consecutive sections were collected on 10 glass slides, one at a time, which resulted in an interval of about 40 μm between adjacent sections on every slide. Slides were fixed for 10 min in ice-cold acetone and rinsed in PBS. One slide was used for routine histologic examination (hematoxylin-eosin staining). The remainder were labelled using primary antibodies, listed in Table I, with one of the following methods: 1) avidin–biotin complex system (Vectastain R, ABC KIT Vector Laboratories, USA) as indicated by the manufacturer and described in ref. 17; 2) biotin–streptavidin FITC amplification system (Amersham, Bucks, England) performed according to the instructions supplied (18); and 3) indirect immunofluorescence (11).

Cell counting

The BL6, BL2, Leu 2a, and Leu 3a positive cells were counted in a Reichert-Jung white light/fluorescence microscope using Videoplan semiautomatic image analyser (Kontron, West Germany). A total surface of the evaluated epidermal sections was measured. The results are expressed as cell number per 1 mm^2 of epidermal section. Statistical analysis was performed using Student's *t*-test.

RESULTS

Immunocompetent cells in psoriatic skin

The BL6-positive epidermal dendritic cells were distributed regularly in the stratum spinosum of NIPS. They were very distinct, medium-sized, with moderately interdigitated

Table I. *Monoclonal (MAb) and polyclonal (PAb) antibodies used in the present study*

Primary antibody	Specificity	Dilution	Appropriate conjugate
BL6 mouse MAb (Immunotech, France)	Cortical thymocytes and Langerhans' cells (19)	1 : 100	Biotinylated horse anti-mouse IgG (1 : 50) for avidin–biotinylated peroxidase complex amplification system (ABC KIT, Vectastatin) (Vector Labs., USA)
BL2 mouse MAb (Immunotech, France)	Monomorphic HLA-DR determinant (20)	1 : 200	
Leu 2a mouse MAb (Becton-Dickinson, USA)	Suppressor/cytotoxic T lymphocytes	1 : 5	Biotinylated goat anti-mouse IgG (1 : 50) for streptavidin–fluorescein amplification system (Amersham, England)
Leu 3a mouse MAb (Becton-Dickinson, USA)	Helper/inducer T lymphocytes	1 : 5	
KL1 mouse MAb (Immunotech, France)	56.5 kD acidic keratin polypeptide (21)	1 : 30	FITC goat anti-mouse IgG (1 : 50) (Nordic, Netherlands)
KM48 mouse MAb (J. Thivolet, Inserm U.209, Lyon, France)	Desmosome and differentiation-related antigen of keratinocyte membranes (22)	1 : 200	FITC goat anti-mouse F(ab')2 (1 : 30) (Nordic, Netherlands)
GP37 guinea pig PAb (J. Thivolet, Inserm U.209, Lyon, France)	37kD cytoplasmic glycoprotein (23)	1 : 30	FITC rabbit anti-guinea pig Igs (1 : 50) (Nordic, Netherlands)
Anti-involucrin rabbit PAb (H. Green, Dept. of Biology, Massachusetts Institute of Technology, Boston, USA)	Involucrin (24) a protein of cross-linking keratinocyte envelopes	1 : 200	FITC goat anti-rabbit Igs (1 : 50) (Nordic, Netherlands)
AKH1 mouse MAb (Biomedica Technologies, USA)	Filaggrin and profilaggrin (17, 25)	1 : 50	Biotinylated horse, anti-mouse IgG (1 : 50) for Vectastain ABC KIT (Vector Labs., USA)

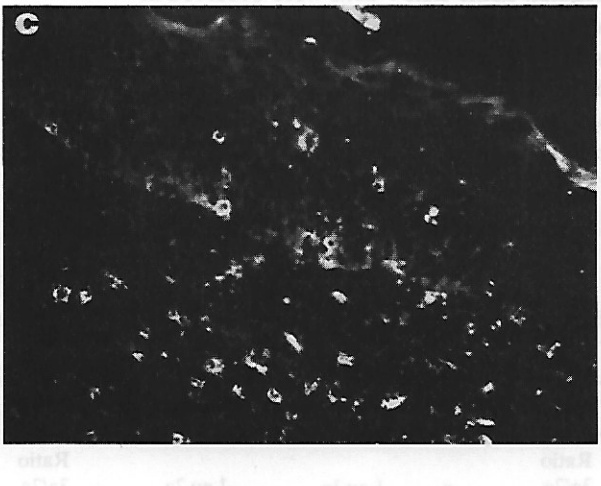

Fig. 1. Clinically non-involved skin from a patient with active (A2), eruptive psoriasis. Focal intra epidermal penetration of HLA-DR-positive cells can be observed (*a*). The adjacent section stained with BL6 shows the immunoperoxidase marker dif fusion and a blurred LC outline in the invaded epidermis. Some BL6-positive cells are present in the dermal infiltrate (*b*). Leu 3a staining in the same location (*c*). Note a peculiarly regular distribution of Leu 3a-positive cells in mid-epidermis. (*a, b*) Brown avidin–biotin–peroxidase reaction products are more distinguishable from the blue counterstain under the microscope than on black and white photographs; to enhance the contrast, the figures have been intentionally underdeveloped. The positive epidermal cells are indicated with arrows and the region of the infiltrate penetration with open arrows. (*c*) Biotin–streptavidin/fluorescein amplification system.

dendrites. The global number of these cells in NIPS was not statistically different from that of controls. However, when the patients with varying disease activity were compared, the highest numbers of epidermal Langerhans' cells were noted in NIPS of the A1 group. Dendritic HLA-DR positive cells were less numerous, but their proportion in the groups with varying disease activity was similar. Foci of infiltrate cells penetrating normal-looking epidermis could be occasionally observed on haematoxylin-eosin-stained sections of NIPS from patients with very active (A2) psoriasis. Immunohistochemical staining of the adjacent sections demonstrated strong BL2 positivity of the infiltrate and a peculiar BL6 reactivity in

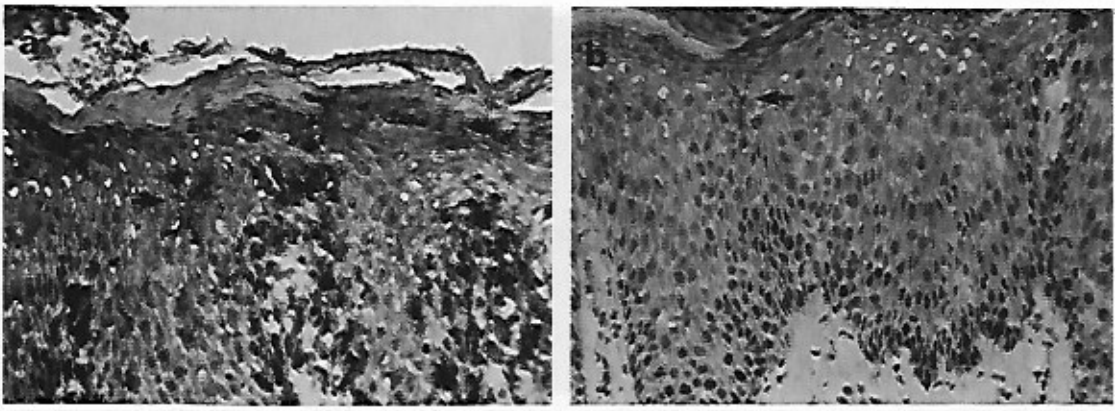

Fig. 2. Only sporadic HLA-DR (*a*) and BL6 (*b*) -positive epidermal dendritic cells persist in well-developed psoriatic lesions (*arrows*).

the invaded epidermis (Fig. 1 *a, b*). BL6-positive cells appeared in clusters, were highly dendritic, with blurred outlines. Sporadic BL6+ cells were also seen in the papillary dermis infiltrate. Intra-epidermal lymphocytes were more numerous in NIPS than in control biopsies and varied according to the disease activity (Table II). Leu 2a+ lymphocytes were predominant in non-active psoriasis and Leu 3a+ prevailed in patients with active form of the disease (A2). Leu 3a+ cells were also the main lymphocyte subset observed in the foci of the subclinical infiltrate of the NIPS (Fig. 1 *c*).

In PP lesions, occurring selectively in A2 patients, epidermal BL6+ cells were decreased in numbers (Table III). Their distribution was irregular. Some BL6+ cells were observed in the dermal papillae. BL2+ cells were more numerous in PP epidermis when compared with the number of BL6+ cells in the same PP lesions. The lesional dermis was filled with BL2+ infiltrate. Leu 3a+ cells prevailed in the PP epidermis (Table II).

In well-developed psoriatic lesions, both BL6+ and BL2+ cell counts were significantly decreased (Table III, Fig. 2 *a, b*). BL2-positive cells were more numerous than BL6+ cells, as was the case with PP lesions, and contrary to the situation usually observed in NIPS and control epidermis. Plaque lesions from patients with non-active disease were mostly infil-

Table II. *Leu 3a and Leu 2a positive cells in psoriatic epidermis (no. of positive cells/1 mm² of epidermal s tion ± standard deviation)*

	Non-involved psoriasis skin				Developed psoriatic lesions			
Activity	*n*	Leu 3a	Leu 2a	Ratio 3a/2a	*n*	Leu 3a	Leu 2a	Ratio 3a/2a
A_0	2	23.0±15.6	119.5±6.4	0.19	3	77.5±49.0	229.5±72.8	0.34
A_1	2	68.5±17.7	90.5±16.3	0.76	3	100.0±17.4	99.7±13.3	1.00
A_2	8	90.4±18.7	56.5±14.8	1.60	5	76.2±88.9	81.6±25.2	0.93
Psoriasis (total)	12	75.5±30.7	72.7±28.6	1.03	11	83.6±29.5	116.6±67.2	0.72
Control	3	8.1±1.2	7.9±1.4	1.03				

n = number of biopsies studied; A_0 = non-active plaque psoriasis; A_1 = peripherally spreading lesions; A_2 = very ac form of psoriasis forming numerous new papules.

Table III. *BL6 and BL2 positive cells in psoriatic epidermis (no. of positive cells/1 mm² of epidermal section ± standard deviation)*

	Non-involved psoriasis skin			Developed psoriatic lesions			Pin-point lesions		
Activity	*n*	BL6	BL2	*n*	BL6	BL2	*n*	BL6	BL2
A_0	2	194±28.5	148±8.2	3	17.7±5.9[b]	58.6±0.5[b]			
A_1	2	320±15.0[b]	268±43[b]	3	69.0±63[b]	132.7±64			
A_2	8	209±53.1	133±26	5	44.1±32[b]	82.6±33[a]	9	128.3±52.7[a]	170.8±73.2
Psoriasis (total)	12	225±63.2	158±58	11	43.7±40[b]	89.6±46[a]	9	128.3±52.7[a]	170.8±73.2
Control	3	206±9.6	146±11.5						

n = number of biopsies studied; A_0 = non-active plaque psoriasis; A_1 = peripherally spreading lesions; A_2 = very active form of psoriasis with numerous new papules.
Statistical significance (*t*-test) when compared with the control values: $a=p<0.05$, $b=p<0.001$.

trated with Leu 2a+ cells, whereas in both types of active psoriasis the numbers of Leu 2a+ and Leu 3a+ cells were nearly identical (Table II).

Expression of epidermal differentiation antigens

Study of non-involved psoriatic epidermis including subclinical foci of infiltrate did not disclose any difference in expression of any of the differentiation antigens investigated. The expression was altered in psoriatic lesions of PP and DPL types, and the degree of this modification was proportional to the stage of the lesion's evolution (Fig. 3). KL1 monoclonal antibody, labelling all but basal layer keratinocytes in NIPS and control biopsies, stained lesional epidermis to a lesser extent. Some suprabasal keratinocytes remained KL1-negative and a lower intensity of IF staining in the upper Malpighian layer could be seen. Involucrin, which occurs in normal, NIPS, and early lesional epidermis in the granular layer and 1–2 adjacent stratum spinosum layers, could be detected additionally in lower prickle cells of well-developed psoriatic lesions. Glycoprotein GP37, specific for stratum granulosum in normal epidermis, was found to be slightly increased in early lesions without parakeratosis but disappeared from well-developed papules. Monoclonal antibody anti-filaggrin and its precursors labelled normal stratum granulosum cells exclusively. From the earliest stages of de-

Pin-point lesions			
n	Leu 3a	Leu 2a	Ratio 3a/2a
9	253.8±151.1	93.1±47.9	2.73
9	253.8±151.1	93.1±47.9	2.73

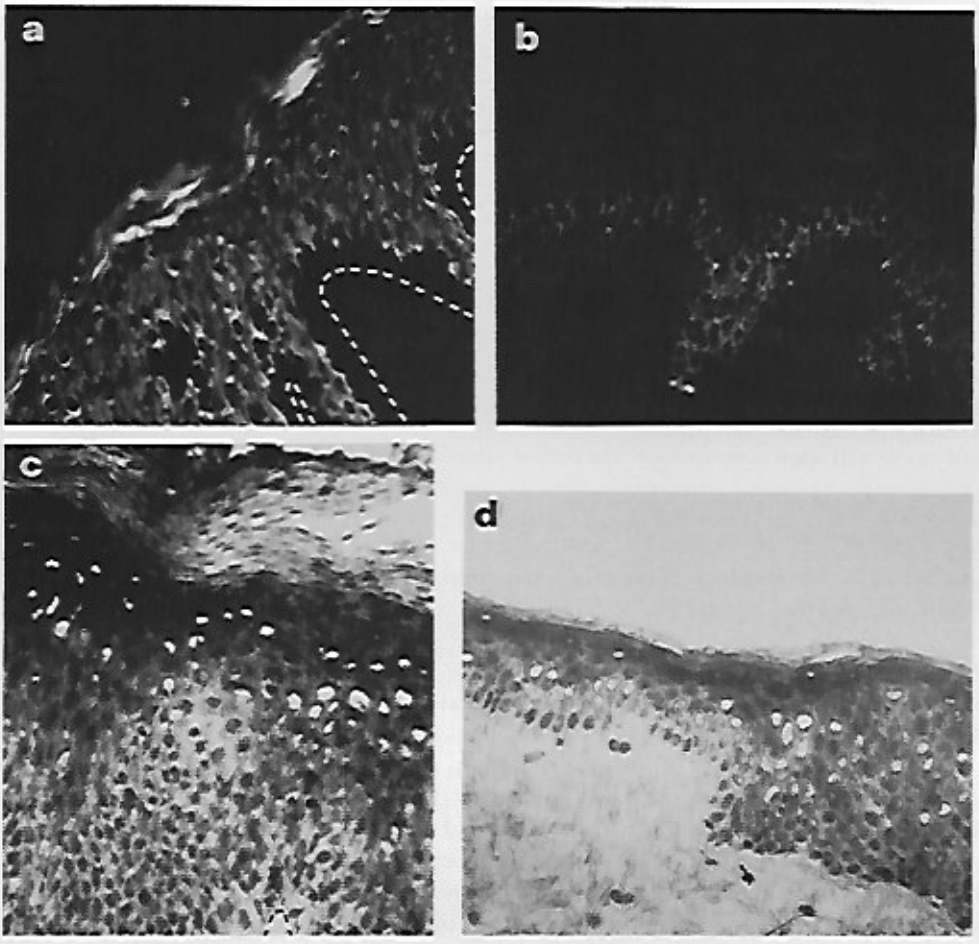

Fig. 3. Differentiation antigens in psoriatic epidermis. (*a*) Decreased intensity of cytoplasmic labelling of lesional keratinocytes with KL1 in the upper epidermis. In addition to the basal layer, some suprabasal cells also remain negative. (*b*) KM48-specific keratinocyte membrane labelling disappears from the lesional upper epidermis. (*c*) Pronounced staining of several keratinocytes in the upper Malpighian layer of a psoriatic plaque (a positive gradient) compared with the exclusive granular layer labelling in non-involved epidermis of the same patient (*d*). (*a, b*) Indirect immunofluorescence. (*c, d*) Avidin–biotin–peroxidase. ——, Dermal–epidermal junction.

velopment of psoriatic lesions we could observe reactivity of anti-filaggrin antibody, not only with some persistent granular layer cells but also with several upper spinal layer keratinocytes. The staining did not persist in parakeratotic stratum corneum. KM48 monoclonal antibody labelled viable layers of normal and NIPS epidermis with the maximum of fluorescence intensity at the granular layer zone. Expression of KM48 antigen in the upper parts of the lesional acanthotic epidermis was markedly decreased.

DISCUSSION

Several publications have dealt with immunocompetent cell distribution and infiltrate typing in psoriatic epidermis (1–5, 9–16) as well as the keratinocyte differentiation and epidermal

antigen expression in psoriatic lesions (23, 26–28). Nevertheless, the exact sequence of events occurring during development of psoriatic papules is still poorly understood.

Our studies on psoriatic epidermis at various stages of the evolution of skin lesions disclosed subclinical foci of intra-epidermal infiltrate occurring in non-involved skin of patients with a very active, eruptive form of the disease. We believe that these changes represent the earliest forms of incipient lesions. In the regions of epidermis invaded by infiltrate, Langerhans' cells appeared somewhat altered, with blurred outlines and dissociated dendrites. Because of the limited surface of these subclinical lesions, we were unable to quantify intra-epidermal immunocompetent cell subsets with enough precision for statistical comparison to be reliable. The PP lesions showed varying degrees of epidermal change, varying from almost normal, slightly acanthotic epidermis to fully developed papules. They contained decreased numbers of BL6+ Langerhans' cells. T-helper lymphocytes prevailed in the dense HLA-DR+ infiltrate which had penetrated the epidermis through the tips of the dermal papillae. The histologic changes and Langerhans' cell depletion were even further accentuated in well-developed papules, whereas the helper/suppressor ratio returned to normal. A decrease in the number of epidermal LCs in developed psoriatic lesions has been reported by several authors (9–11, 14, 29). However, Baker et al. (4, 13) found the contrary. In their double-labelling technique, the HLA-DR(+) but T6(−) intra-epidermal cells with dendritic appearance were taken into account, and groups of dendrites without cell bodies were included in the counts. Our findings concerning lymphocyte subpopulations confirm the results obtained by other authors (1–6). Helper lymphocytes prevailed in early lesions and were predominant in non-involved epidermis of patients with eruptive psoriasis. Application of immunofluorescence amplification techniques was necessary for visualization of Leu 2a- and Leu 3a-positive cells. Therefore, we cannot rule out the possibility that some of the Leu 3a-labelled cells were LCs, known to express some T4 reactivity (30, 31).

Lack of KL1 labelling in some of the suprabasal keratinocytes could result from an increase of the low-differentiated germinative compartment. On the other hand, less intense KL1-dependent staining of the rest of the psoriatic epidermis may be related to a possible alteration of keratinocyte maturation, similar to that observed in malignant epidermal tumours (21). Increased involucrin expression and disappearance of glycoprotein GP37 from lesional epidermis have been previously reported (23, 26). Paucity of filaggrin, a histidine-rich protein forming keratohyalin granules, can be observed morphologically in involved psoriatic epidermis characterized by the absence of a granular layer. It has been proposed that inflexibility and dryness of a parakeratotic stratum corneum results from the absence of filaggrin-derived aminoacids constituting the principal water-retaining ingredient of normal corneocytes (32). Since AKH-1 monoclonal antibody used in our immunohistochemical studies recognizes not only filaggrin but also its precursors (25), the increased AKH-1 reactivity which we observed in lesional epidermis may be attributed to a possible accumulation of profilaggrin in the upper parts of the Malpighian layer. A differentiation- and desmosome-related antigen recognized by KM48 monoclonal antibody was not detected in the upper epidermis of psoriatic plaques. This observation can be partly explained by the absence of the granular layer, which is the most intensely KM48-stained part of normal epidermis. Another explanation involves increased protease activity, described in this region in psoriatic lesions (7, 33, 34), which may be responsible for alteration of cell surface antigen expression.

We can conclude that the modifications in the immunocompetent cell aspect and distribution precede the perceptible structural and antigenic rearrangement of psoriatic epidermis due to hyperproliferation and incomplete differentiation of keratinocytes.

ACKNOWLEDGEMENT

We thank Mr John M. Carew for reviewing the manuscript.

REFERENCES

1. Bos JD, Hulsebosch HJ, Krieg SR, Bakker PM, Cormane RH. Immunocompetent cells in psoriasis. In situ immunophenotyping by monoclonal antibodies. Arch Dermatol Res 1983; 257: 181–189.
2. Bos JD, Krieg SR. Psoriasis infiltrating cell immunophenotype: Changes induced by PUVA or corticosteroid treatment in T-cell subsets, Langerhans' cells and interdigitating cells. Acta Derm Venereol (Stockh) 1985; 65: 390–397.
3. Bjerke JR, Degre M, Haukenes G, Krogh HK, Livden JK, Matre R. T cells, interferons and retrovirus-like particles in psoriatic lesions. Acta Derm Venereol (Stockh) 1984; suppl 113: 9–11.
4. Baker BS, Swain AF, Fry L, Valdimarsson H. Epidermal T lymphocytes and HLA-DR expression in psoriasis. Br J Dermatol 1984; 110: 555–564.
5. Valdimarsson H, Baker BS, Jonsdottir I, Fry L. Psoriasis: a disease of abnormal keratinocyte proliferation induced by T lymphocytes. Immunology Today 1986; 7: 256–259.
6. Braun-Falco O, Kaudevitz P, Rieber P. Characterization of lymphocyte subpopulations in initial and chronic psoriatic lesions by monoclonal antibodies. Acta Derm Venereol (Stockh) 1984; suppl 113: 9–11.
7. Chowaniec O, Jablonska S, Beautner EH, Proniewska M, Jarzabek-Chorzelska M, Rzesa G. Earliest clinical and histological changes in psoriasis. Dermatologica 1982; 163: 42–51.
8. Jablonska S, Chorzelski TP, Beautner EH, Jarzabek-Chorzelska M, Chowaniec O, Maciejowska E, Rzesa G. Autoimmunity in psoriasis. II. Immunologic studies on various forms of psoriasis and Köbner phenomenon. In: Farber EM, Cox AJ, eds. Psoriasis. Proceedings of the Second International Symposium. New York: Yorke Medical Books, 1977: 73–79.
9. Lisi P. Investigation of Langerhans' cells in pathological human epidermis. Acta Derm Venereol (Stockh) 1973; 53: 425–428.
10. Morhenn VB, Abel EA, Mahrle G. Expression of HLA-DR antigen in skin from patients with psoriasis. J Invest Dermatol 1982; 78: 165–168.
11. Haftek M, Faure M, Schmitt D, Thivolet J. Langerhans cells in skin from patients with psoriasis: quantitative and qualitative study of T6 and HLA-DR antigen-expressing cells and changes with aromatic retinoid administration. J Invest Dermatol 1983; 81: 10–14.
12. Koulu L, Söderström KO, Jansen CT. Relation of antipsoriatic Langerhans cells depleting effects of systemic psoralen photochemotherapy: clinical, enzyme, histochemical and electron microscopy study. J Invest Dermatol 1984; 82: 591–593.
13. Baker BS, Swain AF, Griffiths CEM, Leonard JN, Fry L, Valdimarsson H. Epidermal T lymphocytes and dendritic cells in chronic plaque psoriasis: the effects of PUVA treatment. Clin Exp Immunol 1985; 65: 97–101.
14. Czernielewski J, Juhlin L, Shroot S, Brun P. Langerhans' cells in patients with psoriasis: Effect of treatment with PUVA, PUVA bath, etretinate and anthralin. Acta Derm Venereol (Stockh) 1985; 61: 526–534.
15. Haftek M. Langerhans cells in psoriasis: their involvement in the process of development of the pinpoint lesions and in regression of psoriatic plaques under treatment. In: Farber EM, Nall ML, eds. Psoriasis. Proceedings of IV International Symposium. New York: Elsevier Science Publishing Co Inc, 1988.
16. Heng MCY, Kloss SG. Cell interactions in psoriasis. Arch Dermatol 1985; 121: 881–887.
17. Kanitakis J, Zambruno G, Viac J, Thivolet J. Involucrin expression in adnexal skin tumors. An immunological study. Virchow Arch (Pathol Anat) 1986; 408: 527–540.
18. Gielen V, Mauduit G, Schmitt D, Thivolet J. Reactivity of anti-HLA class I polymorphic monoclonal antibodies with normal human skin. Hybridoma 1987; 6: 545–554.
19. Yonish-Ronach E, Schmitt D, Viac J, Knowles R, Cordier G, Brochier J. Monoclonal antithymic cell antibodies detect epidermal cells. Thymus 1984; 6: 67–78.
20. Yonish-Ronach E, Cohen J, Vincent J, Brochier J. Analysis of human B cell membrane antigens by means of monoclonal antibodies. In: Peters M, ed. Proteides of Biological Fluids. Oxford: Pergamon Press, 1983; 30: 478–480.
21. Viac J, Reano A, Brochier J, Staquet MJ, Thivolet J. Reactivity pattern of a monoclonal antikeratin antibody KL1. J Invest Dermatol 1983; 81: 351–353.
22. Haftek M, Viac J, Schmitt D, Gaucherand M, Thivolet J. Ultrastructural quantitation of desmosome- and differentiation-related keratinocyte membrane antigen. Arch Dermatol Res 1986; 278: 283–292.
23. Bernard BA, Reano A, Darmon YM, Thivolet J. Precocious appearance of involucrin and epidermal transglutaminase during differentiation of psoriatic skin. Br J Dermatol 1986; 114: 279–283.
24. Rice R, Green H. Presence in human epidermal cells of soluble protein precursor of the cross-linked envelope: activation of the cross-linking by calcium ions. Cell 1978; 18: 681–684.

25. Dale BA, Grown AM, Flechman P, Vinbal JR, Resing KA. Characterization of two monoclonal antibodies to human epidermal keratohyalin reactivity with filaggrin and related proteins. J Invest Dermatol 1987; 88: 306–312.
26. Bernard BA, Robinson SM, Vandeaele S, Mansbridge JN, Darmon M. Abnormal maturation pathway of keratinocytes in psoriatic skin. Br J Dermatol 1985; 112: 647–651.
27. Mansbridge JN, Knapp AM, Strefling AM. Evidence for an alternative pathway of keratinocyte maturation in psoriasis from an antigen found in psoriatic, but not normal epidermis. J Invest Dermatol 1984; 83: 296–301.
28. Guilhou JJ, Malbos S, Delcalleau D, Meynadier J. Immunofluorescence in psoriasis: Studies of immunoglobulins, complement deposits, and three membrane markers. Arch Dermatol Res 1981; 271: 295–303.
29. Müller SA, Winkelman RK, Vanderstein PR. Langerhans cells and cutaneous nerves in psoriasis: a histological study. In: Farber EM, Cox AJ, eds. Psoriasis. Stanford, California: Stanford University Press, 1971: 187–202.
30. Wood GS, Warner NL, Warube RA. Anti Leu 3/T4 antibodies react with cells of monocyte/macrophage and Langerhans lineage. J Immunol 1983; 84: 212–216.
31. Schmitt D, Faure M, Dambuyant-Dezutter C, Thivolet J. The semi-quantitative distribution of T4 and T6 surface antigens on human Langerhans cells. Br J Dermatol 1984; 111: 655–669.
32. Harding CR, Scott IR. Histidine rich proteins (filaggrins) structural and functional heterogeneity during epidermal differentiation. J Mol Biol 1983; 170: 651–673.
33. Lasarus GS, Yost FJ, Thomas CA. Polymorphonuclear leukocytes; possible mechanism of accumulation in psoriasis. Science 1977; 198: 1162–1168.
34. Glinski W, Jablonska S. Role of polymorphonuclear leukocytes and their neutral proteinases in psoriasis. Acta Derm Venereol (Stockh) 1984; Suppl. 113: 34–37.