

Expression of the High Affinity IgE-Receptor on Human Langerhans' Cells

Elucidating the Role of Epidermal IgE in Atopic Eczema

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Epidermal Langerhans' cells have previously been shown to bear IgE molecules, particularly in atopic dermatitis skin. Using two highly specific antibodies against the antibody-binding chain of the high affinity IgE-receptor, 29C6 and 6F7, we here provide evidence that Langerhans' cells express this receptor in both normal skin (foreskin) and in lesional skin of patients with atopic and stasis eczema. A specific antibody against the low affinity IgE-receptor, Tü1, showed only a low expression of this receptor. This finding has important potential functional implications for the role of Langerhans' cells in transepidermal, IgE-mediated allergy. **Key words:** *FcεRI; FcεRII; Mast cells; α-subunit of FcεRI.*

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It is now generally accepted that airborne allergens can aggravate atopic eczema, most likely by penetrating directly through the epidermal skin barrier from without. The mechanisms involved in such reactions are so far unknown. A major breakthrough in our understanding of them occurred with the demonstration of membrane-bound IgE on epidermal Langerhans' cells (LC) (1), although the nature of this binding and its significance remained unclear. Receptors for IgE on cell membranes are either of the high affinity type (FcεRI), which is present on mast cells and basophils and which mediates release of potent proinflammatory and immunomodulatory molecules from these cells (2). A structurally distinct low affinity type receptor (FcεRII) is present on macrophages, eosinophils, platelets and lymphocytes (3–5). The functional significance of this receptor has not yet been well elucidated.

Table 1. Immunoreactivity of epidermal dendritic cells^a

Antibody/ specificity	Tissue source		
	Normal skin	Atopic eczema	Stasis eczema
T6/LH	12.78 ± 2.54	10.60 ± 2.27	14.10 ± 1.67
29C6/FcεRI	9.50 ± 3.31	12.33 ± 2.92	9.50 ± 1.90
6F7 ^b /FcεRI	6.00 ± 2.79	6.63 ± 1.92	8.90 ± 1.85
Tü1/FcεRII	0.10 ± 0.32	0.67 ± 1.12	1.50 ± 1.58

^aExpressed as means ± 1 SD of counts of nucleated, positively staining cells

^bBinding competitively with IgE to the α-chain of the high affinity receptor

Due to the close ontogenetic relationship between macrophages and LC, it would seem reasonable that the latter would bind IgE via the FcεRII. In the present investigation, using specific antibodies against the antibody-binding α-subunit on the exterior of the cell membrane of mast cells and an antibody against the FcεRII, we were surprised to note that LC of normal and eczematous skin express primarily the high and only very little of the low affinity IgE receptor.

MATERIALS AND METHODS

Tissue was obtained from two adults who were circumcised (normal skin) and from diagnostic biopsies of lesional skin from two patients each with atopic and stasis eczema. Frozen tissue was processed and stained by the APAAP method, as previously described (6), using one antibody each against the CD1 epitope (T6 from Dako, Denmark), specific for LC, and against the FcεRII (Tü1, evaluated for specificity by the myeloid workshop and kindly provided by Prof. Dr. A. Ziegler, FU, Berlin). Two antibodies against the antigen-binding α-chain of the FcεRI (a gift of Dr. J. Hakimi, Nutley, NJ), were employed in the same sections, the one binding competitively with IgE, i.e. only to the unoccupied receptor (6F7), the other binding to all FcεRI (29C6) (7).

Parts of the original tissue were also paraffin-embedded and stained with toluidine blue (8).

Quantitative evaluation was done by counting all nucleated, positively stained epidermal dendritic cells in 4–5 adjacent microscopic fields at 400 × magnification by three different observers. Results are expressed as means ± 1 SD of positive cells/microscopic field in all sections of each disease category and in the normal foreskin.

Serial sections were done to evaluate staining of the cells in the same location with different antibodies. The intensity of staining and the distribution of the positively staining cells were noted by all persons evaluating the sections as well.

RESULTS

Table 1 shows the number of positively stained epidermal dendritic cells in the different tissues. There were no marked differences between the sections from the two patients in each of the three categories studied. As can be seen, T6 and 29C6 marked almost the same number of epidermal dendritic cells. The distribution and the configuration of these cells were identical. Fewer cells stained with the 6F7 antibody, except in stasis dermatitis, and only very few cells reacted with Tü1 against the FcεRII. Sequential sections showed that in all instances, the markers for both FcεR stained T6-positive cells only.

The intensity of staining decreased in the order shown in the table, with T6 being markedly expressed on many dendrites of LC, 29C6 slightly less, 6F7 markedly less and Tü1 only very sparsely and on a few dendrites. In the eczematous skin, there was also marked staining of many dendritic cells with T6 and

29C6 in the dermis, less so with 6F7 and rarely with Tü1, suggesting active trafficking of these cells. Toluidine blue staining showed that mast cells were only present in the dermis.

DISCUSSION

The data presented here show that LC in normal and diseased skin react with antibodies against the α -chain of the Fc ϵ RI. The structure of this receptor is well elucidated (2). It consists of four chains: the outer α -chain, and the internal β - and two γ -chains. The α -chain is the primary binding structure for the Fc portion of the IgE molecule and is, together with the β -subunit, unique for the Fc ϵ RI on mast cells and basophils. The γ -chain is also found with the Fc ϵ RII on macrophages and lymphocytes (9). Since the two different monoclonal antibodies 29C6 and 6F7 used in these studies are highly specific for the α -chain of the Fc ϵ RI on mast cells and basophils (7), it is highly likely that LC in normal and diseased skin express this high affinity IgE-binding receptor. Since toluidine blue-positive cells were not present in the epidermis, mast cells or basophils, which are the classically Fc ϵ RI-bearing cells, cannot explain our findings.

A comparison of the two antibodies directed against the Fc ϵ RI is also of interest (Table I). The 29C6 antibody binds to the receptor irrespective of whether it has IgE bound to it or not. The 6F7 antibody binds competitively and can thus only attach to sites where no IgE is bound. The data in table I suggest therefore that a greater number of Fc ϵ RI is not occupied by IgE on LC, irrespective of whether normal or diseased skin is examined. This would fit with the relatively scarce demonstration of IgE in the LC reported originally (1).

The demonstration of Fc ϵ RI α -chain expression on LC is all the more surprising since recent investigations have shown that Fc ϵ RII is present and can be upregulated on normal human LC by IL4 and/or IFN γ (10). It was thus conceivable that during the process of inflammation in atopic skin, lymphocyte- and keratinocyte-derived cytokines might increase the Fc ϵ RII expression on LC, allowing these cells to bind IgE which could interact with the specific antigens immediately after their penetration into the skin. The present data, using the Tü1 monoclonal antibody against the Fc ϵ RII, suggest that the expression of the Fc ϵ RII is low, compared to the Fc ϵ RI (Table I), and that it is not significantly upregulated in diseased skin.

The physiological and pathological implications of our findings are open to speculation. The IgE on the epidermal LC could provide a highly efficient means of binding potentially harmful allergens immediately after their penetration into the upper layers of the epidermis. Whether this binding also results in the secretion of proinflammatory and immunomodulatory mediators from LC, or even aids in antigen presentation during the process of sensitization, needs to be further elucidated.

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REFERENCES

1. Bruynzeel-Koomen C, van Wichem DF, Toonstra J, Berrens L, Bruynzeel PLB. The presence of IgE molecules on epidermal Langerhans cells in patients with atopic dermatitis. *Arch Dermatol Res* 1986; 278: 199-205.
2. Metzger H. The high affinity receptor for IgE on mast cells. *Clin Exp Allergy* 1991; 21: 269-279.
3. Capron M, Kusnierz JP, Prin L, Spiegelberg HL, Ovlaque G, Gosset P, Tonnel A-B, Capron A. Cytophilic IgE on human blood and tissue eosinophils: Detection by flow microfluorometry. *J Immunol* 1985; 134: 3013-3018.
4. Spiegelberg HL, Boltz-Nitulescu G, Plummer JM, Melewicz FM. Characterization of the IgE Fc receptor on monocytes and macrophages. *Fed Proc* 1983; 42: 124-128.
5. Cines DB, van der Keyl H, Levison AI. In vitro binding of an IgE protein to human platelets. *J Immunol* 1986; 136: 3433-3430.
6. Schadendorf D, Tiedemann K-H, Haas N, Czarnetzki BM. Detection of human papilloma viruses in paraffin-embedded condylomata acuminata - Comparison of immunohistochemistry, in situ hybridization, and polymerase chain reaction. *J Invest Dermatol* 1991; 97: 549-554.
7. Riske F, Hakimi J, Mallamaci M, et al. High affinity human IgE receptor (Fc ϵ RI). Analysis of functional domains of the α -subunit with monoclonal antibodies. *J Biol Chem* 1991; 266: 11245-11251.
8. Czarnetzki BM, Meentken J, Kolde G, Bröcker E-B. Morphology of the cellular infiltrate in delayed pressure urticaria. *J Am Acad Dermatol* 1985; 12: 253-259.
9. Ra C, Jouvin MHE, Blank U, Kinet J-P. A macrophage Fc ϵ receptor and the mast cell receptor for IgE share an identical subunit. *Nature* 1989; 341: 752-754.
10. Bieber T, Rieger A, Neuchrist C, Prinz JC, Rieber EP, Boltz-Nitulescu G, Scheiner O, Kraft D, Ring J, Stingl G. Induction of Fc ϵ R2/Cd23 on human epidermal Langerhans cells by human recombinant interleukin-4 and gamma interferon. *J Exp Med* 1989; 170: 309-314.