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High-affinity immunoglobulin E receptor (FcεRI)-bearing eosinophils, mast cells, macrophages and Langerhans' cells in allergen-induced late-phase cutaneous reactions in atopic subjects

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SUMMARY

We have used *in situ* hybridization (ISH) and immunohistochemistry (IHC) to investigate the kinetics of the expression for FcεRI mRNA (α-, β- and γ-chains), the α-chain protein product, as well as the phenotype of the mRNA- or protein-positive cells in allergen-induced late-phase skin reactions in atopic subjects. Compared with diluent controls, there were significant increases in the total numbers of mRNA$^+$ cells for the α-, β-and γ-chains for FcεRI at all time-points (6, 24 and 48 hr) after allergen challenge ($P<0{\cdot}01$). By double IHC/ISH significant increases in α-, β- and γ-chain mRNA$^+$ macrophages, eosinophils, mast cells and CD1a$^+$ cells were also observed after allergen challenge ($P<0{\cdot}05$). The distribution of FcεRI subunit (α-, β-, or γ-chain) mRNA$^+$ co-localization was CD68$^+$ macrophages (42–47%), EG2$^+$ eosinophils (33–39%), tryptase$^+$ mast cells (5–11%) and CD1a$^+$ Langerhans' cells (2–4%). Using single IHC, significant increases in the total number of FcεRI protein$^+$ cells ($P<0{\cdot}01$) were observed 24 and 48 hr after allergen challenge. Double IHC showed that the distribution of FcεRI$^+$ cells was tryptase$^+$ mast cells (33%), CD68$^+$ macrophages (36%), EG2$^+$ eosinophils (20%), CD1a$^+$ Langerhans' cells (4%) and unidentified cells (7%), at the 24-hr allergen-challenged sites. These observations suggest that the cutaneous late-phase reaction in man is associated with up-regulation of FcεRI on eosinophils, macrophages, mast cells and Langerhans' cells.

INTRODUCTION

Injection of allergen into the dermis of sensitized atopic subjects is associated with an immediate weal and flare reaction which is followed within hours by an oedematous, red and slightly indurated late-phase response (LPR).[1,2] The LPR is dependent on the interaction of allergen with cells bearing surface-bound, allergen-specific immunoglobulin E (IgE).[3,4] High-affinity receptors for IgE (FcεRI) are traditionally associated with mast cells and basophils.[5,6] More recently however, FcεRI has also been described on other cell types including Langerhans' cells, peripheral blood monocytes and eosinophils.[7–11] Interaction of allergen with surface-bound IgE on these cells may result in the release of inflammatory mediators.[10,12,13] In addition, IgE-mediated allergen uptake by antigen-presenting cells may facilitate subsequent presentation of allergen to allergen-specific T cells.[14,15] For these reasons, we have studied first, the kinetics of expression of mRNA for the α-, β- and γ-chains of FcεRI of the various cell-types involved using a combination of *in situ* hybridization (ISH) and immunohistochemistry (IHC); second, the differences in the total number of FcεRI protein$^+$ cells after allergen challenge in the skin of atopic subjects; and third, the phenotype of the various FcεRI protein$^+$ cells using double IHC.

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MATERIALS AND METHODS

Human subjects

Atopic subjects ($n=12$) were recruited from the Allergy Clinic and staff of the Royal Brompton Hospital, London, UK. Inclusion criteria were followed as previously described.[16] Patients taking any oral antihistamine or corticosteroid medication in the 2 weeks before the study began were not included.

Study design and processing of specimens

The study was approved by the Royal Brompton Hospital Ethics Committee and was performed with all subjects' written informed consent. Lyophilized extracts (Aquagen SQ) of either Timothy grass pollen or house dust mite extract (ALK) were reconstituted at 1500 biological units (BU)/ml in isotonic sterile saline diluent. Thirty biological units of either allergen

extract (0·02 ml) were injected intradermally into three sites on the extensor aspect of the forearms of each subject. A fourth site was injected with a similar volume of diluent. The size of the late response was measured at 6 hr, 24 hr and 48 hr by evaluating skin induration.[16] Biopsies were obtained at each time-point and were processed as previously described.[16]

In situ *hybridization*

The cDNA fragments encoding FcεRI α [base pairs (bp) 25–936], β (bp 43–802) and γ (bp 55–475) subunits were kindly provided by Dr J.-P. Kinet (Molecular Allergy and Immunology Section, National Institute of Allergy and Infectious Diseases, Rockville, MD).[17–19] These cDNA fragments of FcεR subunits were inserted into the appropriate vectors (pGEM) (Promega, Southampton, UK) and linearized to produce antisense and sense riboprobes. The ^{35}S-labelled riboprobes were prepared with SP6 or T7 RNA polymerases (Promega) to generate anti-sense or sense probes, respectively. ISH of the sections of skin biopsies were performed as described previously.[16] For each subunit of FcεRI (the α-, β-, or γ-chain), at least two sections from each biopsy were hybridized, from which whole sections (10–19 fields per section, each field = 0·202 mm^2) were counted blind in a coded random order by the two observers. The results are expressed in the numbers of mRNA$^+$ cells per mm^2.

Sequential immunohistochemistry and in situ hybridization

To identify the cell types expressing mRNA for FcεRI subunits, frozen sections were first stained by the alkaline phosphatase–anti-alkaline phosphatase (APAAP) technique using monoclonal antibodies against macrophages (CD68; Dako Ltd, High Wycombe, UK), mast cells (anti-tryptase; Dako), eosinophils (EG2, Sanbio BV, Amsterdam, the Netherlands), Langerhans' cells (anti-CD1a; Ortho Diagnostics, Bucks, UK) and T cells (CD3; Becton Dickinson, Mountain View, CA). After developing with Fast Red (Sigma, Poole, UK), FcεRI α-, β-and γ-chain-specific ISH were performed as mentioned above, incorporating the same negative controls. Using this technique, the cellular markers stained red whereas cells hybridizing with the antisense riboprobes for FcεRI subunits were identified by a dense collection of overlying silver grains.[20] The results are expressed as the numbers of single-positive (cell marker$^+$ or mRNA$^+$) and double-positive cells per mm^2.

Single immunohistochemistry for FcεRI

FcεRI-bearing cells were detected with the murine monoclonal antibodies 22E7 (a kind gift of Drs R. Chizzonite and J. P. Kochan, Hoffman La Roche Inc., Nutley, NJ) directed against the α-chain of FcεRI,[21] using the APAAP method.[1,2] Isotype-matched monoclonal antibodies of irrelevant specificity and omission of primary layer antibodies were included as negative controls. Positive cells stained red after development with Fast Red (Sigma).

IHC was also performed using a rabbit polyclonal antibody to the human FcεRI α-subunit (997, a kind gift of Dr J.-P. Kinet)[22] by APAAP method. The positive cells within the whole sections (see above) were counted and the results are expressed in the numbers of FcεRI$^+$ cells per mm^2.

Double immunohistochemistry

To examine the phenotype of FcεRI α-subunit-bearing cells, cryostat sections were studied by double IHC as described[23] with some modifications. Briefly, after blocking endogenous peroxidase in 3% hydrogen peroxide and pretreatment in 1% bovine serum albumin, mouse anti-human phenotype (CD68, EG2, tryptase, CD1a, or CD3) monoclonal antibodies together with rabbit anti-human FcεRI α-subunit (997) were used simultaneously for the first layer. The second layer consisted of a biotinylated goat anti-mouse antibody (Dako) together with a swine anti-rabbit antibody (alkaline phosphatase-conjugated) (Dako). The third layer was streptavidin horseradish peroxidase (Amersham). Fast Blue and 3-amino-9-ethylcarbazole (AEC; Vector Laboratories, Peterborough, UK); these were sequentially used for the development of the FcεRI α-subunit and cell phenotypes. After development, FcεRI α-subunit-bearing cells stained blue and phenotypes stained red. Double-positive cells stained for both colours. After developing, the sections were counterstained with methyl green. Whole sections were counted blindly by three independent investigators, at high power magnification (×1000), with an eyepiece graticule. The co-localization of 997 staining with the tryptase, CD68, EG2 and CD1a phenotypic markers and the percentages of cells of each phenotype coexpressing FcεRI α-subunit were then calculated.

Statistical analysis

Data were analysed using a statistical package (Minitab Release 7, Minitab Inc., State College, PA). Variability of parameters studied was analysed with Friedman's test, followed by two-by-two comparisons between time points using the Wilcoxon signed rank test. Correlation coefficients were obtained by Spearman's method with correction for tied values. For all tests, *P*-values less than 0·05 were considered significant.

RESULTS

Late-phase response and cell infiltration

All subjects gave a cutaneous LPR after injection of the allergen but not after the diluent saline control ($P < 0{\cdot}002$). The peak of the LPR was reached 24 hr after challenge [mean size (mm) ± SEM = 79·3 ± 5·4], although there were no significant differences between this and the 6 hr (70·5 ± 4·7) or 48 hr (71·6 ± 5·8) time-points.

Using the technique of immunohistochemistry we confirmed that after allergen challenge the numbers of infiltrating EG2$^+$ eosinophils, CD3$^+$ total T cells and CD68$^+$ macrophages were significantly elevated at 6, 24 and 48 hr time-points compared with 24 hr diluent challenge sites (Fig. 1) (Friedman's test, $P < 0{\cdot}05$). The highest infiltration of these cell types was observed at 6, 24 and 48 hr, respectively, which are consistent with our previous studies.[1,2,16] After allergen challenge, the number of tryptase$^+$ mast cells was reduced compared with diluent controls, suggesting degranulation of mast cells. There was no significant change in the number of CD1a$^+$ Langerhans' cells at any time-points studied (Fig. 1).

Expression of FcεRI mRNA and phenotypes of FcεRI mRNA$^+$ cells

Using the technique of ISH, significant increases in the numbers of cells expressing α-, β- and γ-chain mRNA for FcεRI were observed at all time-points after challenge

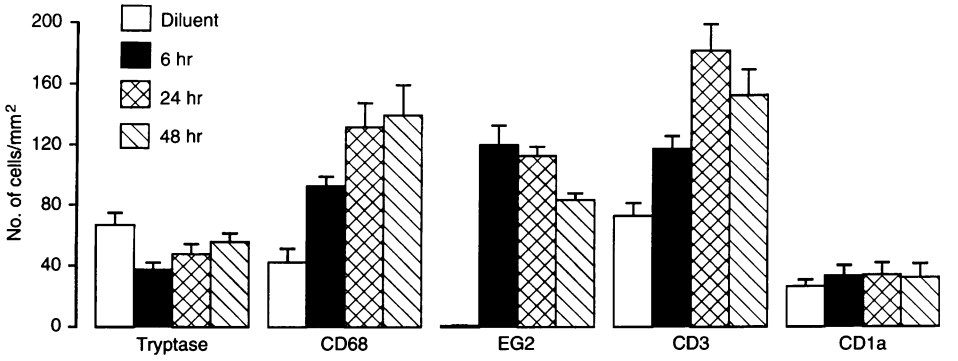

Figure 1. Numbers (mean ± SEM per mm²) of mast cells (tryptase), macrophages (CD68), eosinophils (EG2), T cells (CD3) and Langerhans' cells (CD1a) in cutaneous biopsies from the allergen-induced LPR in atopic subjects.

compared to diluent controls (Friedman's test, $P<0{\cdot}002$) (Fig. 2). The increases in the numbers of cells expressing FcεRI α- and β-chain mRNA were observed as early as 6 hr after challenge (mean ± SEM = 59·0 ± 3·1/mm² and 65·8 ± 7·1/mm², respectively) and peaked at 24 hr (70·6 ± 4·8/mm² and 67·6 ± 2·9/mm²) and significantly declined at 48 hr (547 ± 48/mm² and 562 ± 41/mm²) The peak of the number of γ-chain mRNA⁺ cells was at 6 hr (88·1 ± 4·5/mm²), slightly declined at 24 hr (84·5 ± 5·6/mm²) and significantly declined at 48 hr (56·5 ± 4·6/mm²) but was still higher than diluent controls. FcεRI subunit mRNA⁺ cells were generally located within areas in the upper part of the dermis as well as in the deep reticular dermis. At diluent-challenged sites, there were only few hybridization signals of α (7·7 ± 1·4/mm²), β (6·3 ± 1·2/mm²) and γ (8·7 ± 1·3/mm²) observed (Fig. 2).

Sequential IHC and ISH showed that CD68⁺ macrophages (35–43%), tryptase⁺ mast cells (25–35%) and CD1a⁺ Langerhans' cells (8–9%) were the major sources for α-, β- and γ-chain mRNA⁺ cells in diluent challenged sites (Fig. 3). After allergen challenge, there were significant increases in FcεRI subunit (α-, β- and γ-chain) mRNA⁺ mast cells, eosinophils, macrophages and Langerhans' cells at all allergen-challenged sites (Friedman's test, $P<0{\cdot}05$) (Fig. 3). The distribution of these mRNA⁺ signals was CD68⁺ macrophages (42–47%), EG2⁺ eosinophils (33–39%) and tryptase⁺ mast cells (5–11%). The minor FcεRI subunit mRNA⁺ signals were co-located to CD1a⁺ Langerhans' cells (2·6–4·2%), but not CD3⁺ T cells (except γ-chain: 0·6–1·4%). The remaining FcεRI subunit mRNA⁺ cells (8%) was not identified.

When the data were examined in terms of the percentages of cells of a given phenotype expressing FcεRI mRNA, it was found that only small percentages of total CD68⁺ (6–11%), tryptase⁺ (2–4%), CD1a⁺ (1–4%) and CD3⁺ (0·4% for γ-chain) cells expressed FcεR subunit mRNA at diluent-challenged sites. After allergen challenge, increased percentages of total CD68⁺ (17–38%), EG2⁺ (18–29%), tryptase⁺ (10–15%) and CD1a⁺ (6–9%) cells expressed mRNA for FcεRI α-, β-and γ-chains.

Immunohistochemistry of FcεRI α-chain and phenotypes of FcεRI⁺ cells

The data of single immunohistochemistry with monoclonal antibody 22E7 and polyclonal antibody 997 are shown in Fig. 4. Using Friedman's test, significant variability in the numbers of FcεRI-bearing cells was observed over the time-course with the non-competitive anti-FcεRI antibody 22E7 ($P=0{\cdot}006$) and the polyclonal anti-FcεRI antibody 997 ($P=0{\cdot}003$). Using the Wilcoxon signed rank test significant increases compared with the diluent-injected site were observed with allergen at 24 hr and 48 hr using 22E7 ($P=0{\cdot}007$ and $P=0{\cdot}003$, respectively) or 997 ($P=0{\cdot}007$ and $P=0{\cdot}006$, respectively). No significant differences were observed between diluent- and allergen-challenged sites at the 6 hr time-point, using these antibodies. There were significant correlations between the numbers of 22E7⁺ and 997⁺ cells ($r=0{\cdot}87$; $P<0{\cdot}002$).

Double IHC in 24 hr allergen- and the 24 hr diluent-injected sites showed that there was a significant increase in FcεRI⁺ eosinophils when allergen was compared with diluent ($P=0{\cdot}036$) (Fig. 5a). The increases in FcεRI⁺ mast cells, macrophages and Langerhans' cells were also observed though these were not statistically significant. The distribution of FcεRI⁺ cells amongst CD68⁺ macrophages, tryptase⁺ mast cells, CD1a⁺ Langerhans' cells and EG2⁺ eosinophils is shown in Fig. 5(b). With diluent, the majority of FcεRI⁺ cells were macrophages (50%) or mast cells (47%) and a small proportion were Langerhans' cells (3%). Twenty-four hours after allergen challenge, 36% of FcεRI⁺ cells were macrophages, 33% were mast cells, 20% eosinophils, 4% were Langerhans' cells and 7% were unidentified (Fig. 5b). When results were expressed as a percentage of the various cell types that were FcεRI⁺ (997⁺) the results were 90% mast cells, 44% macrophages and 94% Langerhans' cells were FcεRI⁺ at diluent sites, and 95% mast cells, 71% macrophages, 71% Langerhans' cells and 26% eosinophils at allergen-injected sites.

Examples of single ISH, single IHC and double staining for FcεRI mRNA- and protein-positive cells are shown in Fig. 6.

DISCUSSION

This is the first study investigating the kinetics of the expression for FcεRI mRNA subunits (α-, β- and γ-chains) and the α-chain protein product, as well as the phenotypes of FcεRI-bearing cells in allergen-induced LPR in man. By the use of the technique of ISH we demonstrated that after allergen challenge the mRNA⁺ cells for the α-, β-and γ-chains of FcεRI increased significantly compared with diluent-challenged sites. Double IHC/ISH showed that these increased FcεRI subunit mRNA⁺ cells were mainly CD68⁺ macrophages and EG2⁺ eosinophils (Fig. 3). It remains to be

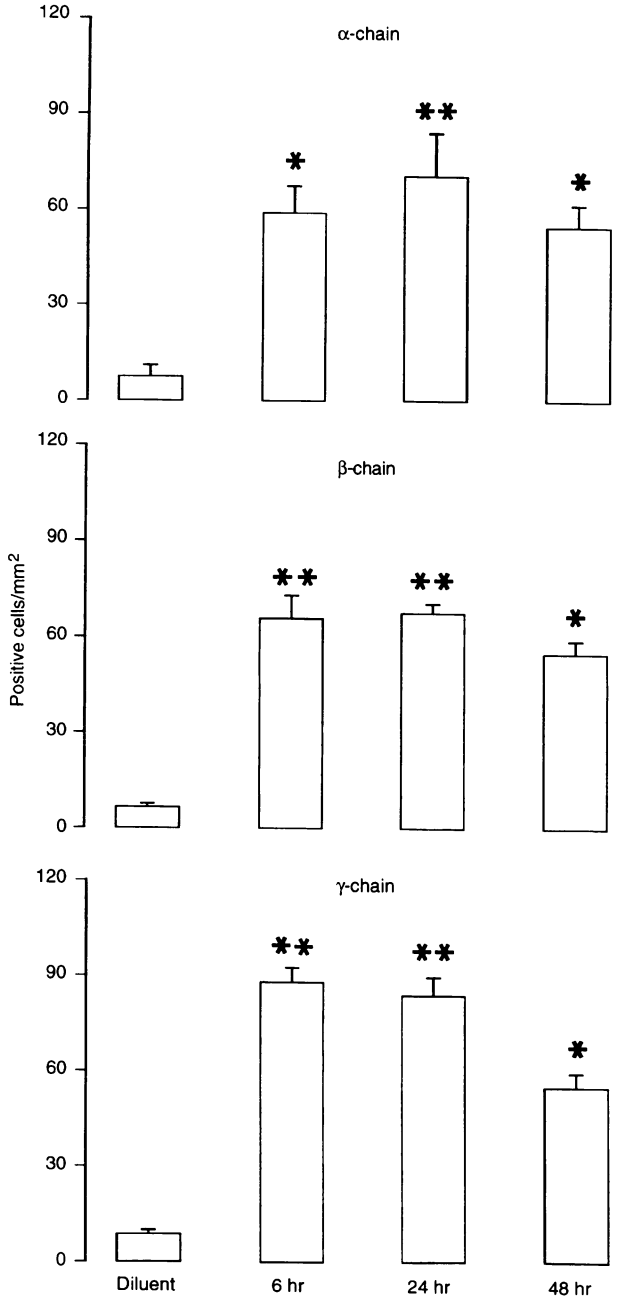

Figure 2. Time-course of the appearance of mRNA$^+$ cells for α-, β- and γ-chains of FcεRI in cutaneous LPR in atopic patients. Diluent-challenged sites were used as controls. Friedman's test showed significant variability for the α-, β- and γ-chain mRNA$^+$ cells (all $P<0{\cdot}002$). Compared with diluent, there were significant increases in α-, β- and γ-chain mRNA$^+$ cells at 6, 24 and 48 hr (all $P<0{\cdot}02$; Wilcoxon signed rank test). *: $P<0{\cdot}05$ (vs. diluent), and **: $P<0{\cdot}05$ (vs. diluent and 48 hr).

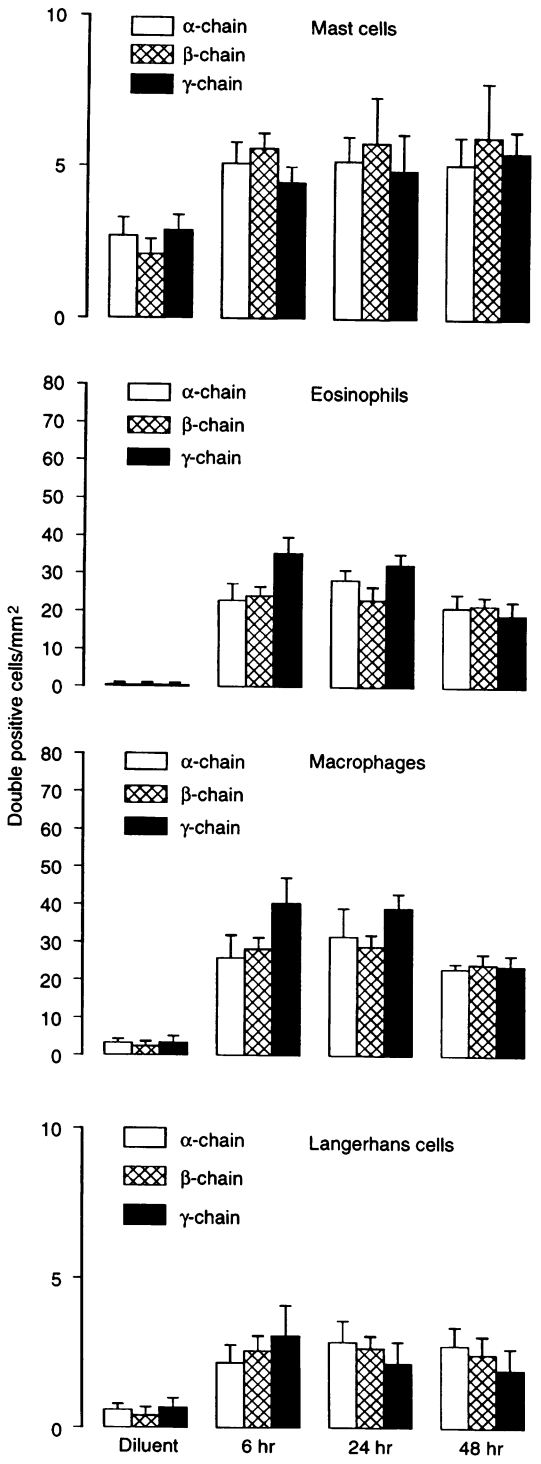

Figure 3. Time-course of the phenotypes of cells (CD68, EG2, tryptase and CD1a) expressing FcεRI mRNA in cutaneous LPR in atopic patients. Diluent-challenged sites were used as controls. Compared with diluent, there were significant increases in the numbers of double positive mast cells (mRNA$^+$/tryptase$^+$), eosinophils (mRNA$^+$/EG2$^+$), macrophages (mRNA$^+$/CD68$^+$) and Langerhans' cells (mRNA$^+$/CD1a$^+$) (Friedman's test, $P<0{\cdot}05$).

determined that the resident macrophages or recruited monocytes contribute to the increased CD68$^+$/mRNA$^+$ cells. However, there were virtually absent EG2$^+$ cells in the diluent-challenged sites. These suggest that the increased FcεRI subunit mRNA$^+$ cells bearing CD68$^+$ or EG2$^+$ markers may be recruited from blood after allergen challenge. These data also suggest that all three subunits of FcεRI were simul-

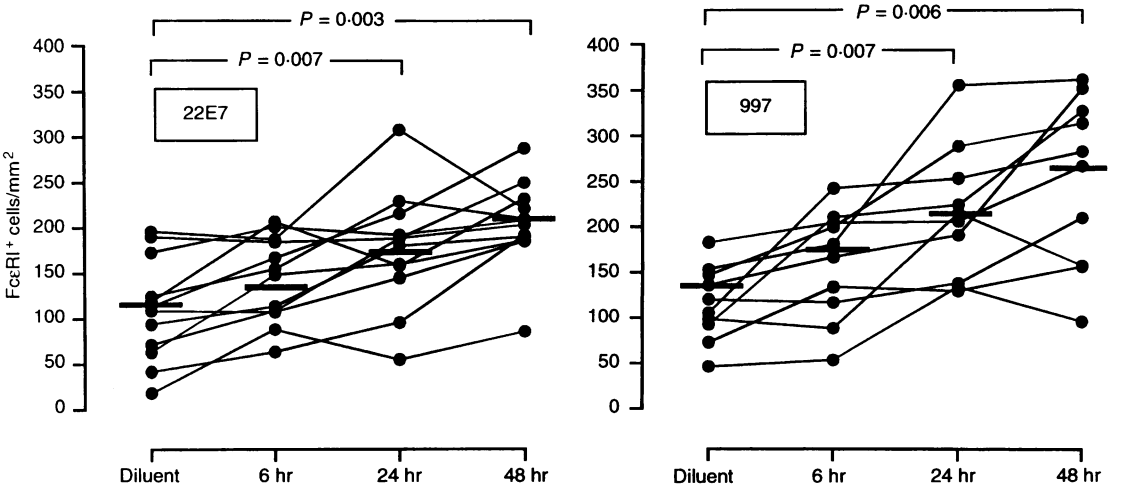

Figure 4. Time-course of appearance of FcεRI$^+$ cells in allergen-challenged skin sites in atopic subjects, as detected by the antibodies 22E7 and 997. Diluent-challenged sites were used as controls. *P*-value shown for 22E7 and 997 concern two-by-two comparisons (Wilcoxon signed rank test). Bars represent median values.

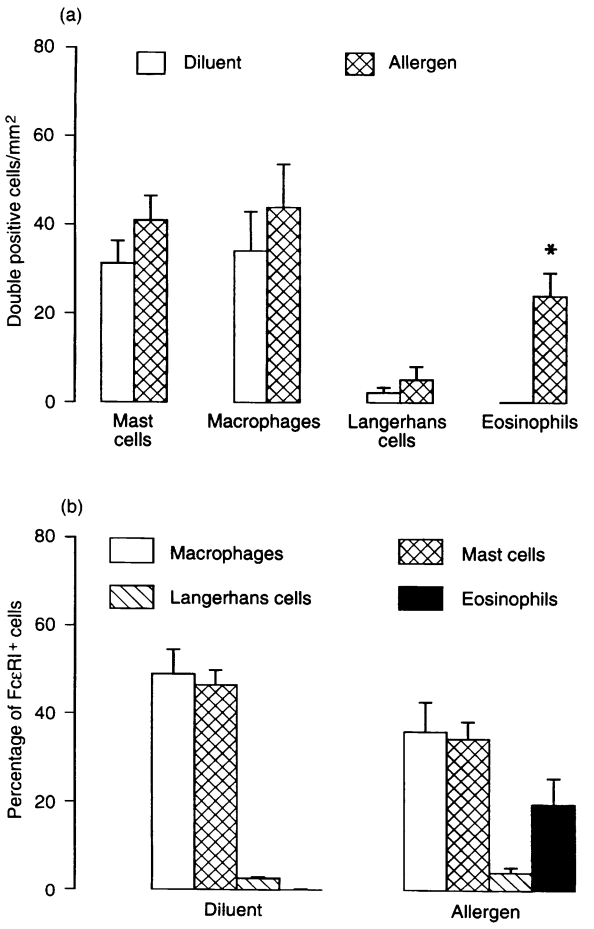

Figure 5. (a) The numbers of tryptase$^+$ mast cells, CD68$^+$ macrophages, CD1a$^+$ Langerhans' cells and EG2$^+$ eosinophils that coexpress FcεRI α chain immunoreactivity (997) in skin biopsies 24 hr after either diluent (open bars) or allergen (solid bars) challenge. The results are expressed as mean ± SEM. * denotes $P = 0{\cdot}036$ (Wilcoxon signed rank test). (b) The percentages of FcεRI$^+$ (997$^+$) cells that coexpress CD68, tryptase, CD1a, EG2 or unidentified immunoreactivity in skin biopsies 24 hr after either diluent or allergen challenge.

taneously transcribed. Using reverse transcription (RT-PCR), the similar mRNA expression for FcεRI subunits has been observed in isolated human alveolar macrophages[24] or eosinophils.[10] Although chimeric receptor consisting of $\alpha\gamma_2$ had a similar function to the native FcεRI ($\alpha\beta\gamma_2$),[25] it has been demonstrated that the γ-dimer functions as an autonomous activation module, while β-functions as a signal amplifier providing a gain of 5- to 7-fold for Syk activation and calcium mobilization.[26]

Immunohistochemistry revealed that FcεRI$^+$ cells are also present in the skin of atopic subjects and that their numbers increased significantly 24 and 48 hr after allergen challenge. In the present study, two fully validated antibodies to the α-chain of FcεRI were used in these studies. These were 22E7 (a mouse monoclonal antibody that does not compete with IgE for binding to FcεRI[8]) and 997 (a rabbit polyclonal antibody[22]). By use of double immunostaining methods applied to skin sections we have identified the principal cell source of FcεRI before and after allergen challenge. In view of the complexity of these procedures we selected one time point (24 hr) for double immunostaining. This was the peak of the LPR and the time of maximal infiltration of several cell types. Double IHC showed the colocalization of FcεRI with mast cells, macrophages, Langerhans' cells and, after allergen challenge, EG2$^+$ eosinophils.

To our knowledge this is the first observation of CD68$^+$ macrophages expressing FcεRI (both mRNA and protein) in the skin of atopic subjects and confirms recent findings of FcεRI-immunoreactive macrophages in bronchial mucosal biopsies from asthmatic patients.[23] Present evidence suggests that FcεRI on macrophages may have functional significance since *in vitro* cross-linking of the receptor has been shown to be associated with sustained intracellular Ca^{2+} release[9] and production of prostaglandin E_2. [13] Additionally, FcεRI on monocytes mediating IgE-dependent allergen-presentations has been reported.[15]

The present results and those in atopic dermatitis,[11] support the concept that a portion of tissue eosinophils are FcεRI$^+$ under conditions of allergen exposure. Furthermore, a small percentage of FcεRI$^+$ eosinophils in bronchial biopsies from

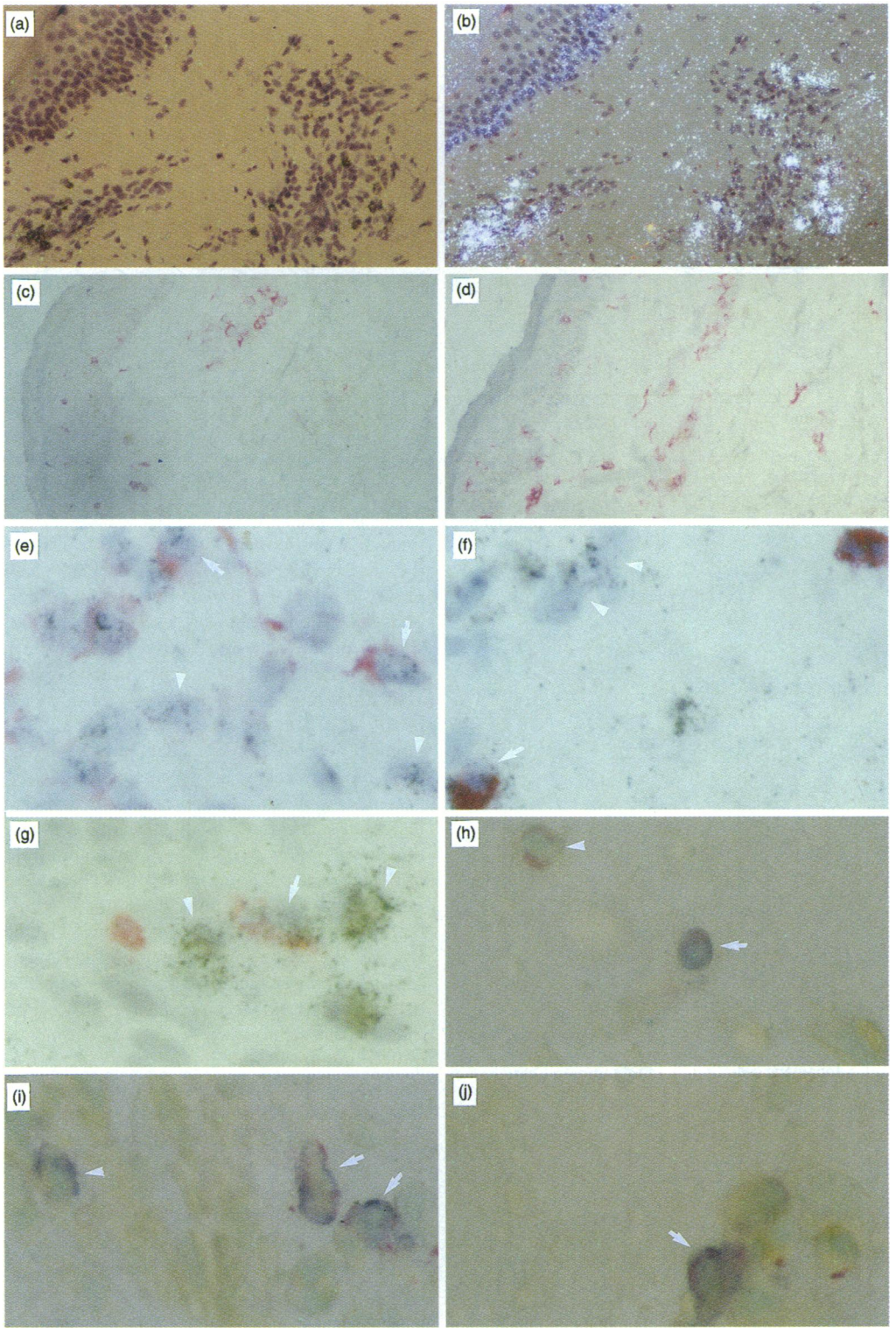

Figure 6. (a–j) Cryostat sections of skin biopsies from an atopic subject after either diluent or allergen intradermal challenge. (a and b) showing single ISH with FcεRI α-chain anti-sense riboprobe in skin biopsy 24 hr after allergen challenge (a, bright field; B, dark field). (c and d) Single immunohistochemistry performed with the antibody 22E7 (c, FcεRI$^+$ cells in the skin, 24 hr after diluent challenge; d, FcεRI$^+$ cells, 24 hr after allergen challenge). (e–g) Double IHC and ISH with FcεRI α-chain riboprobes. (e) CD68$^+$/mRNA$^+$, (f) EG2$^+$/mRNA$^+$, (g) Tryptase$^-$/mRNA$^-$ double-positive cells (arrows) and single mRNA$^+$ cells (arrowheads). (h–j) Showing double IHC performed with the antibody 997 in skin biopsies 24 hr after allergen challenge. (h) A tryptase$^+$/FcεRI$^+$ double-positive mast cell (arrow) and a single tryptase$^+$/FcεRI$^-$ cell (arrowhead) (i) EG2$^+$/FcεRI$^+$ double-positive eosinophils (arrows) and FcεRI α-chain single stained cell (arrowhead) and (j) CD68$^-$/FcεRI$^+$ double-positive macrophage (arrow).

asthmatic subjects at baseline (unchallenged) as well as in nasal mucosa of atopic rhinitis were reported.[23,27] However, using flow cytometry and monoclonal antibodies against the FcεRI α-chain, eosinophils from the peripheral blood of atopic subjects had negligible specific mean fluorescence.[28,29] The mechanism involved in allergen-induced conversion of eosinophils to FcεRI$^+$ cells is unknown but may be dependent on interactions with critical cytokines such as interleukin-3 (IL-3), IL-4, IL-5, granulocyte-macrophage (GM-CSF) or IL-9.[30] A recent report has indeed shown that IL-4 can up-regulate FcεRI α-chain mRNA in human peripheral blood eosinophils.[28] The significance of eosinophils expressing FcεRI remains to be determined. Eosinophils have been shown to act as antigen-presenting cells *in vitro*.[31] High levels of eosinophil-peroxidase can be detected in the supernatant of cultures of eosinophils from patients with hypereosinophilic syndromes incubated with the anti-FcεRI α-chain antibody.[10] Such mechanisms might contribute to the marked degranulation of eosinophils often observed in allergic inflammatory tissue reactions.[1,32,33] Recently a positive correlation between the number of FcεRI$^+$ (997$^+$) eosinophils (but not total eosinophils) and the size of the 24 hr late-phase reaction had been observed in allergen-induced cutaneous LPR.[34] These observations support a role for eosinophils in allergic tissue reactions which involves the high-affinity IgE receptor. On the other hand, Kaneko *et al.* could not induce peripheral blood eosinophils isolated from atopic asthmatic patients to degranulate in the presence of IgE.[35] This stresses the need to obtain FcεRI-bearing eosinophils in free suspension in order to ascertain whether these cells can undergo IgE-dependent exocytosis.

Our present findings confirm previous studies of FcεRI$^+$ Langerhans' cells in the dermis[36] and show that there was a moderate increase in the numbers of dermal FcεRI-bearing CD1a$^+$ Langerhans' cells after allergen challenge (Fig. 3 and Fig. 5). Again, it is not clear whether this represents increased expression of the receptor by resident Langerhans' cells or recruitment of FcεRI$^+$ cells from blood, especially since all dermal CD1a$^+$ cells were located around blood vessels. Dermal CD1a$^+$ cells are extremely potent antigen-presenting cells[37,38] and may be relevant to the mechanism of the LPR, by interacting with allergen-specific T cells.

We did not detect FcεRI- (mRNA or protein) positive T lymphocytes in the dermis after diluent or allergen challenge although there were negligible γ-chain mRNA co-localized to CD3$^+$ cells. This confirms a previous report[39] and suggests that although murine T-cell clones can express mRNA for FcεRI α-, β-and γ-chains, and bind IgE after incubation with IL-9 *in vitro*,[39] T cells present in foci of allergic inflammation *in vivo* may not express sufficient numbers of FcεRI on the cell membrane to be detected by ISH and IHC.

About 8% of the FcεRI$^+$ cells 24 hr post-challenge were unidentified. These may have been basophils, which have been detected in skin windows after allergen challenge.[40] Confirmation or otherwise will require availability of a basophil-specific marker for immunohistochemical studies in tissues.[41]

Although several IgE-dependent effects in allergic inflammation may be mediated through interaction with FcεRI,$^+$ this does not exclude a role for the low-affinity IgE receptor (FcεRII, CD23) in terms of mediator release and allergen uptake and presentation, since monocytes, Langerhans' cells and eosinophils also express CD23.[42,43]

In summary, we have investigated the kinetics of expression of mRNA and protein for FcεRI in allergen-induced cutaneous late-phase reaction. FcεRI$^+$ mast cells, macrophages and Langerhans' cells are present in the skin of atopic subjects and that intradermal allergen challenge is associated with up-regulation of the expression for FcεRI mRNA and protein product in the dermis. These results suggest that these FcεRI-bearing cells may be relevant to the pathophysiology of allergic tissue reactions in terms of mediator release and possibly antigen presentation.

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