Expression of a Functional FcεRI on Rat Eosinophils and Macrophages

David Dombrowicz, Brigitte Quatannens, Jean-Paul Papin, André Capron and Monique Capron

*J Immunol* 2000; 165:1266-1271; doi: 10.4049/jimmunol.165.3.1266

http://www.jimmunol.org/content/165/3/1266

**References**

This article cites 47 articles, 26 of which you can access for free at:

http://www.jimmunol.org/content/165/3/1266.full#ref-list-1

**Subscription**

Information about subscribing to *The Journal of Immunology* is online at:

http://jimmunol.org/subscription

**Permissions**

Submit copyright permission requests at:

http://www.aai.org/About/Publications/JI/copyright.html

**Email Alerts**

Receive free email-alerts when new articles cite this article. Sign up at:

http://jimmunol.org/alerts
Expression of a Functional FceRI on Rat Eosinophils and Macrophages

David Dombrowicz,* Brigitte Quatannens,† Jean-Paul Papin,* André Capron,* and Monique Capron†,‡

Besides its crucial role in type I hypersensitivity reactions, IgE is involved in anti-parasite immunity. This role has been clearly demonstrated in both human and rat schistosomiasis, but remains controversial in the mouse. Since the cellular distribution of the high affinity IgE receptor, FceRI, differs in humans and mice, it might explain the differences in effector function of IgE between the two species. In humans, eosinophils and macrophages induce IgE-dependent cytotoxicity toward Schistosoma mansoni larvae, which involves FceRI in the case of eosinophils. In the present study, we have investigated the expression and function of FceRI in rat eosinophils and macrophages. We demonstrate, by flow cytometry, fluorescence microscopy, and Western blot analysis, that in rats, as in humans, a functional αγ2 trimeric FceRI is expressed on eosinophils and macrophages. We also show that these two cell types can induce IgE-mediated, FceRI-dependent cellular cytotoxicity toward schistosomula. These results thus provide a molecular basis for the differences observed between rat and mouse regarding IgE-mediated anti-parasite immunity. The Journal of Immunology, 2000, 165: 1266–1271.

It is well documented that IgE and FceRI are key players in allergic reactions. Receptor-bearing mast cells and basophils are able to release, upon engagement with IgE and multivalent Ag, inflammatory mediators (histamine, leukotrienes) as well as proinflammatory and immunoregulatory cytokines (1). Besides its expression on mast cells and basophils as an αβγ2 tetramer, FceRI is also expressed on human Langerhans cells (2, 3), monocytes (4), eosinophils (5), and platelets (6). This extended cellular distribution allows IgE and FceRI to be involved in allergen presentation (7) as well as in vitro cytotoxicity reactions (Ab-dependent cellular cytotoxicity; ADCC)² toward parasite targets such as larvae from the trematode parasite Schistosoma mansoni (5, 6).

However, it has been recently demonstrated that murine eosinophils and macrophages did not express FceRI (8, 9), whereas this receptor could be detected on the same cell types in transgenic mice expressing the human FceRIα under the control of its own promoter elements (9, 10).

In rats and humans, resistance against schistosome infections involves, among others, IgE-dependent mechanisms (11). Indeed, several immunoenpidemiological studies have evidenced a negative correlation between IgE levels and rates of reinfection by the three species of Schistosoma that are pathogen for humans: namely S. mansoni (12, 13), S. haematobium (14), and S. japonicum (15). Besides such indirect evidences, a more direct demonstration of the role of IgE in protective immunity was brought both in vitro and in vivo. In humans and rats, IgE was shown to induce ADCC reactions toward schistosome larvae in the presence of eosinophils, monocytes/macrophages, or platelets (11). Furthermore, immunization of rats according to protocols leading to IgE production (16, 17), passive transfer of IgE-rich serum from S. mansoni-infected rats or of anti-S. mansoni rat IgE mAb to naive recipient rats (18) led to a significant level of protection to a challenge infection. Such a protective effect was also observed when platelets (19), eosinophils, or macrophages (20), obtained from infected animals and bearing cytophilic IgE, were transferred to naive rats. In mice, various studies about the protective role of IgE in schistosomiasis have led to divergent conclusions (21–25). IgE and eosinophils have also been associated with resistance against other helminthic parasites, such as Trichinella (26) and Necator (27).

While expression of functional IgE receptors has been demonstrated on rat macrophages and eosinophils (28–31), their molecular nature has not been characterized. Due to the similarities of IgE effector functions in humans and rats in vivo and in vitro and to the contradictory results from the various studies on murine models, we hypothesized that the discrepancies between mice and rats regarding the involvement of IgE in anti-schistosome immunity might be due to differences in the cellular distribution of FceRI.

In the present work we have investigated the cellular distribution and function of FceRI in rat eosinophils and macrophages. Our results provide the first explanation for the long-lasting controversy about the rat vs the mouse as an animal model for parasitic infections.

Materials and Methods

Abs and reagents

Anti-rat FcRRIα Abs were gifts from Dr. R. P. Siraganian (National Institutes of Health, Bethesda, MD; BC4) (32) and Dr. T. J. Flemming and J.-P. Kinet (Harvard, Boston, MA; 3A92). Both Abs are mouse IgG1. Mouse monoclonal anti-rat FcRβ (JRK) (33), which also recognizes mouse FcRβ, and the anti-FcRγ rabbit antiserum (no. 934) recognizing human, murine, and rat molecules (34) were also provided by Dr. J.-P. Kinet. Anti-human CD23 antisera (Rb 103A) recognizing rat CD23 (35) was provided by Dr. J.-Y. Bonnefoy (Geneva, Switzerland). IgE from rat myeloma (IR 162), biotinylated IR 162, and anti-rat IgE (MARE-1) were obtained from LO-Immex (Louvain, Belgium).

Copyright © 2000 by The American Association of Immunologists

0022-1767/00/$02.00
S. mansoni cycle

A Puerto Rican strain of S. mansoni was maintained in Biomphalaria glabrata snail as the vertebrate intermediate host and in the golden hamster, Mesocricetus auratus, as the vertebrate definitive host. Skin schistosomula for cytotoxicity (ADCC) experiments were collected in MEM after application of cercariae to isolated pieces of Swiss mouse abdominal skin for 3 h.

Animals and treatments

Lou rats (8–16 wk old) were kept and bred in the facility of the Institut Pasteur de Lille. Unless specified otherwise, animals were i.p. injected with 5 ml of thioglycolate (5%). Six-month-old animals were used for peritoneal mast cell purification.

Cells

Rat basophil leukemia (RBL-2H3) cells were kept in complete RPMI medium supplemented with 10% FCS. Rat peritoneal cells were obtained, 4 days after thioglycolate injection by lavage of the peritoneal cavity with PBS and were directly analyzed by flow cytometry with anti-FcR

Eosinophils (60–80% purity estimated after May-Grünwald staining) obtained by removal of adherent cells (mainly macrophages) after overnight culture in complete RPMI medium with 10 ng/ml recombinant human IL-5 were used for ADCC experiments. For receptor up-regulation experiments, cells were maintained for 4 days in complete RPMI medium supplemented with 10 ng/ml human IL-5 in the presence or the absence of 5 μg/ml rat IgE, then analyzed by flow cytometry.

Macrophages were obtained as adherent cells after 30-min plating and were used in ADCC experiments. Purity was typically 90–95%. Mast cells from 6-mo-old naive rats were purified on a 22% metrizamide gradient (36). Purity estimated on cytospin preparations after May-Grünwald staining was 97%.

Flow cytometry

Unless specified otherwise, all incubations for staining were performed on 2.5 × 10^6 cells in 100 μl with 10 μg/ml Ab at 4°C for 30 min in PBS containing 0.1% BSA and 0.05% sodium azide. Eosinophils and macrophages were identified on the basis of their forward and side scatter. FcεRI expression was analyzed by binding of either unlabeled rat IgE revealed with biotinylated mouse anti-rat IgE and PE-conjugated streptavidin (St-PE, 5 μg/ml) or with biotinylated rat IgE and St-PE after incubation with 150 μg/ml nonspecific rat IgG, then analyzed by flow cytometry.

Purity estimated on cytospin preparations after May-Grünwald staining was 97%.

Immunofluorescence

Purified populations of FcεRI-positive eosinophils and macrophages were obtained by sorting peritoneal cells according to their forward and side scatter and their positivity for FcεRI, using an ELITE cell sorter (Coulter, Hialeah, GL), after surface staining performed as described above. The purity of sorted cells was assessed on cytopsin preparations after staining with May-Grünwald (RAL, Martillac, France). Purity was 100% for eosinophils and 98% for macrophages. Sorted cells were fixed with 2% paraformaldehyde, then washed with PBS before mounting. Preparations were observed with a ×63 Plan-Apochromat objective on an Axioshot 2 microscope (Zeiss, New York, NY) equipped with a digital camera.

Western blot

Subunit composition of the receptor on eosinophils and macrophages was analyzed by Western blot on purified populations obtained by sorting of unlabeled peritoneal cells from thioglycolate-injected rats. Sorted eosinophils and macrophages as well as control purified peritoneal mast cells from naive 6-mo-old animals and BRL cells were resuspended in PBS containing 0.1% BSA and 0.5% sodium azide at a concentration of 10^6 cells/ml and incubated with 150 μg/ml nonspecific rat IgG and a 1/100 dilution of anti-CD23 antibody. Cells were incubated with 10 μg/ml biotinylated rat IgE, washed with PBS, then lysed in 1% digitonin (Gallager and Schlessinger Carle Place, NY) as previously described (9, 37). As a preclearing step, lysates were first incubated with agarose beads for 1 h. Surface-expressed receptors were then immunoprecipitated with avidin-agarose beads. Pooled material (9.3 × 10^6 eosinophils, 8.6 × 10^6 macrophages) obtained from three sorting experiments (12 rats) as well as 5 × 10^6 RBL and 3.6 × 10^6 purified peritoneal mast cells were loaded on a 14% reducing SDS-PAGE (for detection of FcεRI and FcγRII). After transfer on polyvinylidene difluoride membrane, samples were probed with anti-FcεRI (1/250 dilution) and anti-FcγRII (1/5000 dilution). HRP-conjugated secondary Abs were revealed by chemiluminescence using SuperSignal (Pierce, Rockford, IL) according to the manufacturer’s protocol.

FcεRIα was detected in lysates from 5 × 10^5 eosinophils, 6.5 × 10^5 macrophages, 5 × 10^5 RBL, and from 3.6 × 10^6 purified peritoneal mast cells (used as a control) after sequential immunoprecipitation with normal rabbit serum bound to protein A-Sepharose (preclearing) and with anti-FcεRI antibody bound to protein A-Sepharose. Immunoprecipitated material was loaded on an 8% nonreducing gel, transferred on polyvinylidene difluoride, then probed with anti-FcεRIα (BC4, 1/2500 dilution).

Ab-dependent cellular cytotoxicity

Effector cells (4 × 10^5; eosinophils or macrophages) were incubated in flat-bottom 96-well plates for 5 h with a 1/20 dilution from serum from infected rats (containing 5 μg/ml IgE) or with serum from uninfected animals (as a control) in 100 μl of complete RPMI medium. Schistosomula (100 larvae) were then added to the effector cells in a final volume of 200 μl. Some cell samples were preincubated with 150 μg/ml anti-FcεRIα or with normal mouse IgG before the addition of rat serum. Additional controls were performed by incubating the cells with anti-FcεRI in the absence of serum or with infected rat serum depleted in IgE by overnight incubation at 4°C with 30 μg/ml anti-rat IgE adsorbed to protein A-Sepharose beads. Cytotoxicity was estimated 48 h later and was expressed as the percentage of dead schistosomula evaluated microscopically. Experiments were performed in duplicate.

Results

Expression of FcεRI by rat eosinophils and macrophages

The expression of FcεRI by peritoneal eosinophils or macrophages from normal rats was investigated by flow cytometry using rat myeloma IgE. The experiments were performed after saturation of FcεRγs. IgG receptors, and FcεRII/CD23, the low affinity IgE receptor, with an excess of unlabeled IgG and anti-CD23 Ab, respectively. Under these conditions no IgE binding could be detected on any cell type (data not shown), suggesting that FcεRI was not expressed or was undetectable on these resting cells.

We next analyzed peritoneal cells 4 days after the injection of thioglycolate. As in the mouse, eosinophils and macrophages were easily and accurately identified on the basis of their forward and side scatter parameters. Eosinophils (15–20% of the total peritoneal cells) were small and displayed the highest granularity (38), whereas macrophages (70–80%) were the largest cells in the peritoneum (39) (Fig. 1a). Mast cells were virtually absent from the peritoneum from these animals (1% or less of the peritoneal population). A small eosinophil subpopulation (~5%) exhibited strong IgE binding, which was completely inhibited by preincubation of cells with anti-FcεRIα mAb (Fig. 1b). Two different anti-FcεRIα mAb gave similar results. These findings indicate that rat eosinophils are able to express FcεRI. Likewise, a higher proportion (20–30%) of macrophages could bind IgE, and this binding was very significantly inhibited by preincubation with anti-FcεRIα Abs (Fig. 1c).

However, the mean fluorescence intensity, reflecting the receptor number, was about 4-fold lower than that for eosinophils. FcεRI-positive eosinophils and macrophages were then sorted according to both scatter and fluorescence parameters and were examined by microscopy. Purified populations (98–100% purity) were very homogenous in size and aspect. After May-Grünwald staining, eosinophils appeared small, with a highly granular and eosinophilic cytoplasm and a doughnut- or eight-shaped nucleus...
Macrophages were much larger, with prominent cytoplasmic vacuoles (Fig. 1e). No contaminating granulated mast cells could be detected on either preparation.

Purified peritoneal mast cells from 6-mo-old naive animals (Fig. 1f) and RBL cells (Fig. 1g), used as a control, displayed much higher FcεRI expression when stained using the same experimental procedure.

FcεRI-positive eosinophils and macrophages were analyzed by immunofluorescence microscopy (Fig. 2). As observed on peritoneal mast cells and RBL cells, a typical speckled pattern of fluorescence was detected on both sorted eosinophils and macrophages. As expected, expression levels in these two populations were lower than that in the cell line.

**FcεRI molecular structure**

To determine whether FcεRI was expressed as a trimeric αγ2 or a tetrameric αβγ2 structure on eosinophils and macrophages, the presence of FcεRβ and FcεRγ was examined by flow cytometry after cell permeabilization with saponin, using specific anti-FcεRβ and anti-FcεRγ Ab (Fig. 3). FcεRβ was detected in neither eosinophils nor macrophages (Fig. 3, a and c), in contrast to peritoneal mast cells and RBL cells (Fig. 3, e and g). This further confirms that the gated eosinophil and macrophage populations did not contain mast cells, which do express an αβγ2 receptor. By contrast, FcεRγ, which also associates with FcεRI and FcεRIII, was virtually detected in 100% eosinophils and macrophages (Fig. 3, b and d). As expected, peritoneal mast cells and RBL cells were positive for both FcεRβ and FcεRγ (Fig. 3, e–h).

To confirm that the receptor expressed by eosinophils and macrophages was lacking FcεRβ, we analyzed the structure of surface-expressed receptors by Western blot on purified populations. Purified eosinophils and macrophages as well as peritoneal mast cells and RBL cells were incubated with biotinylated rat IgE, as described for flow cytometry. After lysis with digitonin, a very mild detergent known to preserve noncovalent associations between the receptor subunits (9), immunoprecipitation was performed using avidin-agarose beads. After SDS-PAGE, the membrane was probed with anti-FcεRI and anti-FcεRI Abs. As observed by flow cytometry after permeabilization, FcεRβ was detected on neither eosinophils nor macrophages, while a strong band corresponding to FcεRβ was detected in the lysate from RBL and mast cells (Fig. 4, middle part). On the other hand, two bands, probably corresponding to unphosphorylated and phosphorylated forms of FcεRγ (40), were detected on both eosinophils and macrophages (Fig. 4, lower part). Due to the higher receptor expression in peritoneal mast cells and RBL and to the increased detergent stability of the tetrameric receptor compared with the trimeric structure (9), the signal corresponding to FcεRγ in the RBL and mast cells was much stronger (Fig. 4, lower part). A faint signal at a m.w. corresponding to FcεRγ was also present on the control samples. We then confirmed the association of FcεRIα with FcεRγ in these cells by detection of the former after immunoprecipitation with the anti-

**FIGURE 1.** Surface expression of FcεRI on eosinophils and macrophages. a–c, Flow cytometric analysis of peritoneal cells 4 days after thioglycolate injection. a, Scatter representation. b and c, FcεRI expression on gated eosinophils (b) and macrophages (c). Binding of rat IgE is detected with biotinylated anti-rat IgE and St-PE in the presence or the absence of preincubation with anti-rat FcεRIα. d and e, May-Grunwald staining of cytospin preparations of sorted FcεRI-positive eosinophils (d) and macrophages (e). f and g, Flow cytometric analysis of purified peritoneal mast cells from naive rats (f) and RBL cells (g).

**FIGURE 2.** Immunofluorescence microscopy analysis FcεRI-positive cells. Sorted eosinophils and macrophages, purified peritoneal mast cells, and RBL cells were stained as described in Fig. 1 and were visualized by fluorescence microscopy.
toneal cells, purified peritoneal mast cells, and RBL cells were fixed and



Thus, ligand up-regulation of Fc receptors occurred for rat eosinophils.



Results indicated that surface expression of the receptor on rat and mouse mast cells was up-regulated by IgE in vitro and in vivo (42–45), we investigated whether IgE was able to increase FcRI expression on rat eosinophils in vitro. Therefore, peritoneal cells were cultured for 4 days in the presence of IL-5 to prevent eosinophil apoptosis, with or without IgE. Eosinophils were then analyzed by flow cytometry. Cells kept in culture for 4 days without IgE almost completely lost FcRI expression, as observed for mouse mast cells (45) (Fig. 5a), whereas in the presence of IgE, about 50% of the eosinophil population was expressing FcRI, albeit at a lower level than freshly isolated cells (Fig. 5b). Thus, ligand up-regulation of FcRI, or at least prevention of receptor loss, may also occur for rat eosinophils.

**FcRI expression in eosinophils and macrophages**

As in humans, FcRI expression on eosinophils and macrophages, even after stimulation by thioglycolate injection, appeared relatively low compared with that on mast cells. Since it has been shown that surface expression of the receptor on rat and mouse mast cells was up-regulated by IgE in vitro and in vivo (42–45), we investigated whether IgE was able to increase FcRI expression on rat eosinophils in vitro. Therefore, peritoneal cells were cultured for 4 days in the presence of IL-5 to prevent eosinophil apoptosis, with or without IgE. Eosinophils were then analyzed by flow cytometry. Cells kept in culture for 4 days without IgE almost completely lost FcRI expression, as observed for mouse mast cells (45) (Fig. 5a), whereas in the presence of IgE, about 50% of the eosinophil population was expressing FcRI, albeit at a lower level than freshly isolated cells (Fig. 5b). Thus, ligand up-regulation of FcRI, or at least prevention of receptor loss, may also occur for rat eosinophils.

**FcRI-mediated ADCC by rat eosinophils and macrophages**

We then investigated whether the engagement of the receptor expressed by eosinophils and macrophages could lead to a functional response. As previously reported for human eosinophils and macrophages (5, 46), we used ADCC toward S. mansoni larvae as the more relevant functional parameter. Peritoneal eosinophils or macrophages, purified from thioglycolate-injected rats, were incubated with schistosomula and serum from S. mansoni-infected rats containing anti-schistosoma IgE Abs or with serum from noninfected animals as a negative control. In some samples the role of IgE depletion, anti-FcRI Ab, or control mouse IgG was studied. When IgE-containing serum was used, the percentage of cytotoxicity reached 40–75% for eosinophils (Fig. 6a) and 30–92% for macrophages (Fig. 6b). Preincubation of effector cells with anti-FcRI Ab led to an inhibition of cytotoxicity ranging, in the different experiments, from 29.5 to 100% (average, 74.1%) for eosinophils (Fig. 6a) and from 42.3 to 57.3% (average, 50.3%) for macrophages (Fig. 6b). Likewise, IgE depletion by incubation of the serum with anti-rat IgE-coated beads led to a 50% inhibition of macrophage cytotoxicity (Fig. 6b). No inhibition was observed when IgE-containing serum was used, the percentage of cytotoxicity reached 40–75% for eosinophils (Fig. 6a) and 30–92% for macrophages (Fig. 6b). Preincubation of effector cells with anti-FcRI Ab led to an inhibition of cytotoxicity ranging, in the different experiments, from 29.5 to 100% (average, 74.1%) for eosinophils (Fig. 6a) and from 42.3 to 57.3% (average, 50.3%) for macrophages (Fig. 6b). Likewise, IgE depletion by incubation of the serum with anti-rat IgE-coated beads led to a 50% inhibition of macrophage cytotoxicity (Fig. 6b). No inhibition was observed when IgE-containing serum was used.
Role of FcεRI in IgE-mediated ADCC by eosinophils and macrophages toward S. mansoni larvae. Peritoneal eosinophils (a) and macrophages (b) from thioglycolate-injected rats were incubated in duplicate with serum containing 5 μg/ml IgE, with normal rat serum, with anti-FceRIα Ab, then with IgE-rich serum or with IgE-depleted serum. Schistosomula were added 5 h later. Mortality was estimated in three (a) or four (b) independent experiments after 48 h and was expressed as a percentage of dead schistosomula (±SD).

Discussion

In this paper, we have shown by flow cytometry, immunofluorescence microscopy, and Western blot analyses that a fraction of thioglycolate-elicited rat macrophages and eosinophils could express FceRI. This expression could not be mistaken for mast cell expression, since this population accounts for a very low proportion of the peritoneal cells of these treated animals, and since FceRI expression on mast cells is much higher than that on eosinophils and macrophages. Cell sorting further prevented potential contamination by mast cells. FceRI expression was detected on neither eosinophils nor macrophages from unstimulated animals, suggesting that receptor expression in cells other than mast cells is very low or absent in resting conditions. This could explain why the receptor was not detected in earlier works, including our studies.

As described for mouse mast cells and basophils, receptor expression was up-regulated on eosinophils by incubation with its ligand. A very strong adherence of macrophages to culture wells during the 4-day incubation prevented us from assessing the phenomenon in this cell type. This regulatory mechanism would provide a way for the organism to optimally respond to IgE-mediated stimulation as it occurs in immediate hypersensitivity reactions or during parasitic infections.

IgE-dependent cytotoxicity toward schistosomula has been reported in previous studies for rat macrophages, eosinophils, and platelets. Experiments using an mAb directed toward human eosinophils and cross-reactive with B cell CD23 suggested that the low affinity IgE receptor, FceRII/CD23, was mainly involved in this process. However, the role of FceRI was not investigated, since FceRII/CD23 was for a long time considered to be the only IgE receptor identified on these cell types in both rats and humans. The recent demonstration that FceRI expressed on human eosinophils or platelets was involved in ADCC (5, 6) led us to re-examine its function in the rat.

In the present study, we demonstrate that a subpopulation of rat eosinophils and macrophages expressed a functional FceRI, involved in IgE-mediated cytotoxicity against S. mansoni larvae.

Interestingly, using specific Abs, flow cytometric analyses on permeabilized cells and Western blot experiments failed to reveal the presence of the FcR β-chain in these cell types, while the FcR γ-chain was detected. These results contrast with the previous finding that rat FcR β-chain was required for receptor expression on transfected COS-7 cells. Differences between the simian immortalized cell line and freshly isolated rat cells or the presence of a β-like chain in these latter might explain this discrepancy. The trimeric αγ2 structure of FceRI expressed by rat eosinophils and macrophages is identical not only with that found on the corresponding human cell types but also with that found on their counterparts in transgenic mice expressing the human FcεRI under the control of its own promoter region. Sequencing and comparison of rat, mouse, and human FcεRI promoter regions should allow determination of the respective roles played in the three species by FcRβ and by the FcεRIα promoter regions in the determination of FcεRI cellular distribution.

Taken together, these results clearly indicate a different cellular distribution of the high affinity IgE receptor between humans and rats, on one hand, and mice, on the other hand. Further studies are needed to investigate the genomic organization of the promoter regions in each species and their consequences on gene expression. Our findings provide thus a molecular basis to the similarities found between rat and human during S. mansoni infection. They also underline that the restricted cellular distribution of FceRI in mice, in particular its absence on eosinophils and macrophages, hampers the use of such an animal model for an accurate study of IgE- and FceRI-mediated human pathologies such as allergic reactions. Cellular distribution of FceRI in animal models commonly used for in vivo studies of allergic reactions, such as guinea pig, rabbit, and dog, would therefore be worth investigating.

Acknowledgments

We thank Drs. R. P. Sieraganian (National Institutes of Health, Bethesda, MD) and T. J. Fleming and J.-P. Kinet (Harvard Medical School, Boston, MA) for providing us with anti-rat FcεRIα Abs. We thank Drs. R. Le Borgne, Y. Rouillé, and B. Hofflacq for their help with fluorescence microscopy.

References

1. Ravetch, J. V., and J. P. Kinet. 1991. Fc receptors. Annu. Rev. Immunol. 9:457.
2. Bieber, T., H. de la Salle, A. Wollenberg, J. Hakimi, R. Chizzonite, J. Ring, D. Hanau, and C. de la Salle. 1992. Human epidermal Langerhans cells express the high affinity receptor for immunoglobulin E (FcεRI). J. Exp. Med. 175:1285.
3. Wang, B., A. Rieger, O. Kilgus, K. Ochiai, D. Maurer, D. Fodinger, J. P. Kinet, and G. Stingl. 1992. Epidermal Langerhans cells from normal human skin bind monomeric IgE via FcεRI. J. Exp. Med. 175:1353.
23. Jankovic, D., E. Fiebig, B. Reining, B. Wolf-Winski, M. H. Jouviv, O. Kilgus, J. P. Kinet, and G. Stingl. 1994. Expression of functional high affinity immunoglobulin E receptors (FCεRI) on monocytes of atopic individuals. J. Exp. Med. 179:745.

24. King, C. L., J. Xianli, I. Malhotra, S. Liu, A. A. Mahmoud, and H. C. Oettgen. 1998. Human mast cell FcεRI is involved in defence against parasites. Nature 397:183.

25. El Ridi, R., T. Ozaki, and H. Kamiya. 1998. Schistosoma mansoni infection in IgE-producing and IgE-deficient mice. J. Parasitol. 84:171.

26. Desseyn, A. J., W. L. Parker, S. L. James, and J. R. David. 1981. IgE antibody and resistance to infection. I. Selective suppression of the IgE antibody response in rats diminishes the resistance and the eosinophil response to Trichinella spiralis infection. J. Exp. Med. 153:423.

27. Pritchard, D. I., R. J. Quinnell, and E. A. Walsh. 1995. Immunity in humans to Necator americanus: IgE parasite weight and fecundity. Parasite Immunol. 17:11.

28. Capron, A., J. P. Dessaint, M. Capron, and H. Bazin. 1975. Specific IgE antibodies in immune adherence of normal macrophages to Schistosoma mansoni schistosomules. Nature 253:474.

29. Capron, A., J. P. Dessaint, M. Joseph, R. Rousseaux, M. Capron, and H. Bazin. 1977. Interaction between IgE complexes and macrophages in the rat: a new mechanism of macrophage activation. Eur. J. Immunol. 7:315.

30. Capron, M., H. Bazin, M. Joseph, and A. Capron. 1981. Evidence for IgE-dependent cytotoxicity by rat eosinophils. J. Immunol. 126:1764.

31. Capron, M., T. Jouault, L. Prin, M. Joseph, J. C. Ameisen, A. E. Butterworth, J. P. Papin, J. P. Kusnerz, and A. Capron. 1986. Functional study of a monoclonal antibody to IgE Fc receptor (FcεRII) of eosinophils, platelets, and macrophages. J. Exp. Med. 164:72.

32. Basciano, L. K., E. B. Berenstein, L. Knaak, and P. R. Spiragnet. 1986. Monoclonal antibodies that inhibit IgE binding. J. Biol. Chem. 261:11823.

33. Rivera, J. J., P. P. Kinet, J. Kim, C. Pacilio, and H. Metzger. 1988. Studies with a monoclonal antibody to the β subunit of the receptor for high affinity for immunoglobulin E mol. Eur. J. Immunol. 25:647.

34. Letourneau, O., I. C. Kennedy, A. T. Brini, J. R. Ortaldo, J. J. O’Shea, and J. P. Kinet. 1991. Characterization of the family of dimers associated with Fc receptors (FcεRI and FcγRIII). J. Immunol. 147:2652.

35. Flores-Romo, L., J. Burke, D. R. Ash, J. F. Gauchat, G. Ayala, B. Aller, M. Chavez, H. Bazin, et al. 1993. Inhibition of an in vivo antigen-specific IgE response by antibodies to CD23. Science 261:1038.

36. James, S. L., R. W. Leid, Jr., and A. Sher. 1979. Purification of rodent eosinophils on discontinuous metrizamide gradients. J. Immunol. Methods 27:373.

37. Dombrowicz, D., V. Flamand, I. Miyajima, J. V. Ravetch, S. I. Nishikawa, and J. A. Hamilton. 1998. Functional study of a monoclonal antibody to IgE Fc receptor (FcεRII) for limiting amounts of FcεRI and γ chains. J. Clin. Invest. 99:915.

38. Nolfiz, G., Z. Qin, M. Kopf, and T. Blankenstein. 1998. Neutrophils but not eosinophils are involved in growth suppression of IL-4-secreting tumors. J. Immunol. 160:345.

39. Chan, J., J. P. Leenew, I. Bertoccolo, S. I. Nishikawa, and J. A. Hamilton. 1998. Macrophage lineage cells in inflammation: characterization by colony-stimulating factor-1 (CSF-1) receptor (c-Fms)-ER-MP58, and ER-MP20 (Ly-6C) expression. J. Immunol. 160:1243.

40. Adamczewski, M., R. P. Numusor, G. A. Koretzky, and J. P. Kinet. 1995. Regulation by CD45 of the tyrosine phosphorylation of high affinity IgE receptor β and γ chains. J. Immunol. 154:3047.

41. Letourneau, O., I. C. Kennedy, A. T. Brini, J. R. Ortaldo, J. J. O’Shea, and J. P. Kinet. 1991. Characterization of the family of dimers associated with Fc receptors (FcεRI and FcγRIII). J. Immunol. 147:2652.

42. Flores-Romo, L., J. Burke, D. R. Ash, J. F. Gauchat, G. Ayala, B. Aller, M. Chavez, H. Bazin, et al. 1993. Inhibition of an in vivo antigen-specific IgE response by antibodies to CD23. Science 261:1038.

43. James, S. L., R. W. Leid, Jr., and A. Sher. 1979. Purification of rodent eosinophils on discontinuous metrizamide gradients. J. Immunol. Methods 27:373.

44. Dombrowicz, D., V. Flamand, I. Miyajima, J. V. Ravetch, S. I. Nishikawa, and J. A. Hamilton. 1998. Functional study of a monoclonal antibody to IgE Fc receptor (FcεRII) for limiting amounts of FcεRI and γ chains. J. Clin. Invest. 99:915.

45. Nolfiz, G., Z. Qin, M. Kopf, and T. Blankenstein. 1998. Neutrophils but not eosinophils are involved in growth suppression of IL-4-secreting tumors. J. Immunol. 160:345.

46. Chan, J., J. P. Leenew, I. Bertoccolo, S. I. Nishikawa, and J. A. Hamilton. 1998. Macrophage lineage cells in inflammation: characterization by colony-stimulating factor-1 (CSF-1) receptor (c-Fms)-ER-MP58, and ER-MP20 (Ly-6C) expression. J. Immunol. 160:1243.