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Human Basophils Secrete IL-3: Evidence of Autocrine Priming for Phenotypic and Functional Responses in Allergic Disease

John T. Schroeder,2 Kristin L. Chichester, and Anja P. Bieneman

Although IL-3 is commonly recognized for its growth factor-like activity, in vitro studies have long demonstrated a unique capacity for this cytokine to also augment the proinflammatory properties and phenotype of human basophils. In particular, basophils secrete mediators that are hallmarks in allergic disease, including vasoactive amines (e.g., histamine), lipid metabolites (e.g., leukotriene C₄), and cytokines (e.g., IL-4/IL-13), which are all markedly enhanced with IL-3 pretreatment. This priming phenomenon is observed in response to both IgE-dependent and IgE-independent stimulation. Additionally, IL-3 directly activates basophils for IL-13 secretion and enhanced CD69 expression, two markers that are elevated in allergic subjects. Lymphocytes are commonly thought to be the source of the IL-3 that primes for these basophil responses. However, we demonstrate herein for the first time that basophils themselves rapidly produce IL-3 (within 4 h) in response to IgE-dependent activation. More importantly, our findings definitively show that basophils rapidly bind and utilize the IL-3 they produce, as evidenced by functional and phenotypic activity that is inhibited in the presence of neutralizing anti-IL-3 receptor (CD123) Abs. We predict that autocrine IL-3 activity resulting from low-level IgE/FcεRI cross-linking by specific allergen represents an important mechanism behind the hyperreactive nature of basophils that has long been observed in allergic disease. The Journal of Immunology, 2009, 182: 2432–2438.

The role of basophils in the pathogenesis of allergic inflammatory diseases is best defined by the fact that these cells secrete three key classes of inflammatory mediators, including vasoactive amines (e.g., histamine), lipid metabolites (e.g., leukotriene C₄), and cytokines (e.g., IL-4/IL-13) (1, 2). These substances, which are all hallmarks in allergic inflammation, are sequentially released by basophils especially in response to stimuli that cross-link the high-affinity IgE receptor (FceRI) on the surfaces of these cells (e.g., as allergen binds to specific IgE). Additionally, there is mounting evidence that components linked to both adaptive and innate immunity influence this so-called IgE-dependent activation, either in a positive or negative manner. In particular, in vitro studies have long demonstrated that IL-3, more so than any other factor known to date, markedly increases basophil responsiveness in the release of these mediators and does so for a variety of stimuli. Moreover, IL-3 directly induces IL-13 production by basophils without the need for costimulation (3, 4). In vitro studies using human adult stem cells and in vivo studies in nonhuman primates have also demonstrated that IL-3 is critical for both basophil development and survival (5, 6). Of course, these activities of IL-3 are mediated through receptors (CD123) highly expressed on basophils, which are retained on these cells throughout their development and maturation from bone marrow precursors. Thus, in light of the importance of IL-3 in regulating essentially every aspect of basophil biology, it seems appropriate to infer that this growth factor/cytokine likewise plays an important role in the pathogenesis of allergic disease.

It has long been thought that activated T cells provide the IL-3 responsible for augmenting the pro-allergic functions of basophils. In particular, T cells secrete IL-3 upon activation through the TCR or by agonists that mimic the signaling associated with this mode of activation. Likewise, other hematopoietic cells, including NK cells, mast cells, and some megakaryocytic cells, have all been reported to secrete this cytokine and therefore may also contribute (7). However, we demonstrate herein for the first time that basophils themselves rapidly produce IL-3 when activated through the IgE receptor. More importantly, our findings definitively show that basophils rapidly bind and utilize the IL-3 they produce, as evidenced by functional and phenotypic activity that is inhibited in the presence of neutralizing anti-IL-3 receptor (CD123) Abs. Overall, we predict that this autocrine activity of IL-3 plays a critical role in the “priming” phenomenon that has long been observed among basophils from allergic individuals.

Materials and Methods

Basophil purification

Venipuncture was performed on consenting adults (age range, 21–55 years) using a protocol approved by the Western Institutional Review Board (Seattle, WA). With the exception of the basophils used in Fig. 3C, donors were not selected based on allergic status. In some instances, preparations also included cells procured from residual cell packs from anonymous subjects undergoing platelet pheresis within the Hemapheresis Unit at Johns Hopkins University. In all cases, mixed leukocyte suspensions were subjected to double-Percoll (1.075/1.081 g/ml) density centrifugation, which produced a basophil-enriched cell (BEC)3 interface accumulating on top of the 1.081 g/ml density, as previously described (8). After first removing the bulk of cells floating on the 1.075 g/ml Percoll, the BEC
Human basophils up-regulate IL-3 mRNA expression following IgE-dependent activation. A, Basophils isolated from blood (≥97% purity) were stimulated 1 h with several doses of polyclonal anti-human IgE (anti-IgE). Total RNA was analyzed using real-time RT-PCR. Values shown are after normalizing to the housekeeping gene HPRT using the equation \(10^{-\Delta\Delta Ct}\). B, Induction of IL-3 mRNA tracks with histamine release resulting from anti-IgE stimulation. Basophils from 18 different subjects were stimulated 1 h with 10–20 ng/ml anti-IgE. Percentage total histamine release was calculated as the mean ± SEM fold induction of IL-3 mRNA expression (above medium control).

**RNA isolation**

Total RNA was isolated from 0.25–1.0 × 10^6 basophils using the RNA-Bee protocol (Tel-Test). Following isopropanol precipitation, RNA was washed with ethanol and nearly dried under vacuum. The RNA was then resuspended in DNase-free water and stored below 70°C.

**Quantitative RT-PCR for detection of IL-3 mRNA**

IL-3 mRNA expression in basophils was quantified using real-time RT-PCR as previously reported (10). Briefly, single-step real-time RT-PCR was performed in an ABI 7300 thermocycler using TaqMan reagents (PerkinElmer). Primer/probe combinations for IL-3 included: forward primer, 5′-TTCTTAAAATCTCCTGCCATGTCT-3′; reverse primer, 5′-CATTCCAGTCACCGTCCTTGAT-3′; and probe, 5′-CCGCACTCCCTGGCGTCGT-MGB. Expression of IL-3 was normalized to hypoxanthine phosphoribosyltransferase (HPRT), which was determined using the following primer/probe sequences: forward primer, 5′-GGGCCGGCTCCGTTA-3′; reverse primer, 5′-TTAGGTATGCAAAATAAATCAAGGTCAT-3′; and probe, 5′-CCGCAGCCCTGGCGTCGT-MGB.

**Flow cytometry**

Direct staining of the cell surface activation marker protein CD69 on fixed (buffered 4% paraformaldehyde) basophils was achieved with a PE-conjugated Ab and by using appropriate isotype control methods. Single-color flow cytometry was performed using a FACS Calibur machine. Results are reported as mean fluorescence intensity (MFI) after subtracting values obtained with isotype control Abs.

**Culture conditions**

For the secretion of cytokines, basophils were cultured in IMDM (IMDM, 5% FCS, 1× nonessential amino acids, and 5 μg/ml gentamicin), as described (9). In experiments investigating IL-3 mRNA expression, cells were instead cultured in opened 1.5-ml polypropylene tubes inserted into 15-ml culture tubes. This facilitated the extraction of RNA without having to first transfer cells from culture plate wells. Cell cultures were initiated by incubating the basophils for 15 min to equilibrate to 37°C, 5% CO2. In experiments investigating IL-3 mRNA expression, cells were instead cultured in opened 1.5-ml polypropylene tubes inserted into 15-ml culture tubes. This facilitated the extraction of RNA without having to first transfer cells from culture plate wells. Cell cultures were initiated by incubating the basophils for 15 min to equilibrate to 37°C, 5% CO2. An equal volume of stimulus (2×) was then added and the cells were cultured for specific time points. A mixture of Abs against the α (clone 32703; R&D Systems) and β (clone EP1037T; Epitomics) subunits of the IL-3 receptor (CD123) was added along with stimulus. This enabled the detection of secreted IL-3, since it effectively blocked this cytokine from binding to its highly expressed receptors on basophils (see Fig. 2). By neutralizing bioactivity, the anti-IL-3 receptor Ab mixture (IL-3R Ab) also allowed assessment of
whether basophil-derived IL-3 mediated autocrine effects on function and phenotype.

Cytokine measurements

An ELISA protocol for the detection of IL-13 (eBioscience) has been described previously (9). An in-house ELISA was developed to detect IL-3 protein. This involved coating wells of 96-well plates (eBioscience) with 0.100 ml of rat anti-human IL-3 mAb (clone BVD8-3G11; BD Pharminogen) at a concentration of 2.5 μg/ml in PBS for overnight at room temperature (RT) (23°C). Plates were then washed four times before blocking with 0.150 ml of assay buffer (eBioscience) for 1 h at RT. Wells were once again washed three times before adding 0.050 ml of culture supernatant samples and IL-3 standards (BioSource International/Invitrogen) for 2 h at RT. Wells were then washed four times before adding 0.100 ml of biotinylated rat anti-human IL-3 mAb (clone BVD3-1F9; BD Pharmingen) at a concentration of 250 ng/ml in assay buffer for 1 h. Wells were again washed four times before adding 0.100 ml of avidin-HRP (eBioscience) at 1/1000 dilution for 30 min at RT in the dark. Plates were washed six times before developing with the addition of 0.100 ml of TMB substrate for 15 min at RT in the dark. Reactions were stopped by adding 0.05 ml of 2 N H2SO4 and read at 450/570 nm using a microplate ELISA reader (model 550; Bio-Rad). The sensitivity of this assay was 3 pg/ml and had been standardized to a commercial plate (BioSource International/Invitrogen).

Histamine release

Portions of the cell-free supernatants taken from the basophil cultures after 1 h of incubation were assayed for histamine using automated fluorometry, as previously described (9). Results are expressed as a percentage of the total histamine content, which was determined by taking a proportionate number of basophils and lysing in 1.6% perchloric acid.
Human basophils produce IL-4 and IL-13 in response to IgE/activation. Human basophils generate IL-3 following IgE-dependent activation between 51% and 100% histamine in response to stimulation with the same polyclonal goat anti-human IgE Ab reagent (anti-IgE) that has long been used for activating basophils for cytokine secretion (11). FIGURE 5. IgE-dependent IL-3 secretion by basophils promotes IL-13 secretion through autocrine activity. Basophils prepared from eight different subjects were cultured for 16 h with and without anti-IgE and in the presence or absence of IL-3R Ab (2 µg/ml). Supernatants were then harvested and assayed for IL-3 (A) and IL-13 (B) protein by ELISA. C, The relationship between the levels of IL-3 and IL-13 detected in these supernatants. D, Control experiments showing that IL-3-dependent IL-13 secretion is inhibited by the IL-3R Ab but not by the isotype control. Values are the mean ± SEM (n = 5).

Statistical analysis
Data are presented as means ± SEM unless otherwise indicated. Statistical analysis was performed with Prism4 software (GraphPad Software) and involved the use of the paired t test unless otherwise stated. Values of p ≤ 0.05 were considered significant.

Results
Human basophils generate IL-3 following IgE-dependent activation
Human basophils produce IL-4 and IL-13 in response to IgE/FceRI-dependent activation. Therefore, we investigated first whether IL-3 is similarly induced in these cells following stimulation with the same polyclonal goat anti-human IgE Ab reagent (anti-IgE) that has long been used for activating basophils for cytokine secretion (11). Fig. 1A shows real-time RT-PCR data for IL-3 mRNA expression in unstimulated basophils compared with those activated 1 h with several doses of anti-IgE. In each instance, mRNA levels were increased relative to HPRT expression, even though responses varied among the three pilot experiments (range, ~15- to 1400-fold). As predicted, optimal induction of IL-3 in basophils occurred at a concentration of anti-IgE (~10 ng/ml) that is reported to be optimal for IL-4 secretion but suboptimal for mediator release (11).

With the optimal anti-IgE dose being narrowed to ~10 ng/ml, we investigated whether there is a relationship between the induction of IL-3 mRNA expression and responsiveness to anti-IgE as it pertain to histamine release. As shown in Fig. 1B, there was a wide range in the induction of IL-3 mRNA (~2- to nearly 9000-fold) to challenge with anti-IgE for 1 h among the basophils isolated from 18 different subjects. More importantly, these IL-3 responses were directly related to the percentage of histamine released in the same cultures. For example, IL-3 mRNA levels among basophil suspensions releasing <10% histamine to anti-IgE averaged just 4.8 ± 1.9-fold above control responses (n = 3). In contrast, those releasing between 51% and 100% histamine in response to stimulation showed an ~1000-fold greater induction (4737 ± 2154, n = 3) in IL-3 mRNA.

Initial attempts to detect IL-3 protein in culture supernatants from activated basophils were negative. However, knowing that the IL-3 receptor (CD123) is expressed at very high levels on basophils led us to hypothesize that any IL-3 that is secreted might actually be rapidly absorbed by the basophil and thus be undetected in supernatant. To test this, we spiked cultures (0.250 ml) containing increasing numbers of basophils with recombinant IL-3 (1000 pg/ml). A duplicate set of cultures also received a mixture of anti-IL-3 receptor Abs (IL-3R Ab) that prevents IL-3 binding to both the α and β subunits of the receptor. After incubating 16 h, cell-free supernatants were measured for IL-3 protein content. As shown in Fig. 2A, ~700 pg/ml of IL-3 was detected in control cultures devoid of basophils. However, only ~50% of this IL-3 value (~350 pg/ml) remained after culturing with as few as 1 × 10⁵ basophils, and <20% was recovered in the presence of 5 × 10⁵ basophils. As predicted, a saturating concentration (2 µg/ml) of IL-3R Ab prevented this apparent absorption of IL-3, with 80–85% of the control levels recovered in the presence of up to 5 × 10⁵ basophils. An additional experiment shown in Fig. 2B confirmed these observations and further revealed that isotype controls for the IL-3R Ab mix did not prevent basophils from absorbing IL-3.

We then reevaluated the capacity of basophils to secrete IL-3 protein by adding IL-3R Ab at the time of activation and for the entire culture incubation. As shown in Fig. 3A, this approach immediately resulted in the detection of IL-3 protein in basophil cultures activated with anti-IgE. In fact, levels were detectable and nearly half-maximal within 2 h after activation, had essentially peaked to 91 ± 22 pg/10⁶ basophils by 4 h, and remained sustained at 115 ± 43 pg/10⁶ after 16 h of incubation. Importantly, IL-3 protein was not detected in cultures treated with the IL-3R Ab mix alone, confirming that these Abs were not simply inducing cytokine production. Additionally, increases in IL-3 mRNA preceded the time course observed for the secretion of this cytokine. As shown in Fig. 3B, up to 15-fold greater levels were seen within 15 min after activation, compared with basophils cultured in medium alone. By 1 h, IL-3 mRNA levels had peaked and averaged
Basophils were also investigated for IL-3 secretion in response to allergen. Fig. 3C shows results from a representative experiment where basophils isolated from a cat allergic subject secreted detectable levels of IL-3 following stimulation with a cat extract (Holister Steer). As expected, these basophils also secreted histamine in response to the cat allergen (data not shown).

**Induction of IL-3 in basophils using non-IgE-dependent stimuli**

We next determined whether basophils generate IL-3 in response to a variety of stimuli, including common basophil secretagogues (i.e., C5a, FMLP, PMA, ionomycin) but also to the TLR ligands peptidoglycan (PGN) and LPS. As expected, histamine was released (Fig. 4C) in basophil cultures stimulated with C5a (37 ± 4%), FMLP (53 ± 4%), PMA (64 ± 10%), and ionomycin (31 ± 5%). However, responses to PGN and LPS were no different from values seen with medium control (>3%). As shown in Fig. 4A, IL-3 mRNA levels were the greatest among the cultures stimulated with ionomycin, averaging some 1000 ± 250-fold greater than those in the medium control. In contrast, induction of IL-3 message was typically <10-fold above control values with all other stimuli, even those causing histamine release (i.e., C5a and FMLP). Fig. 4B indicates that this was also observed at the level of IL-3 secretion. In this instance, only ionomycin induced detectable levels of IL-3 in cultures stimulated for either 4 h (457 ± 27 pg/10⁶ basophils) or 24 h (4844 ± 2784 pg/10⁶ basophils) in the presence of IL-3R Ab.

**Basophil-derived IL-3 mediates autocrine priming for functional and phenotypic responses**

Considering the overwhelming evidence that IL-3 influences basophil function, we addressed whether the secretion of this cytokine following IgE-dependent activation mediates autocrine activity that additionally affects basophil function and/or phenotype. With regard to function, we focused on whether using the IL-3R Ab would affect IL-13 secretion, a response that is directly induced in basophils exposed to IL-3. Basophils from eight different subjects were stimulated with anti-IgE or medium alone in the absence and presence of IL-3R Ab. Cultures were incubated for 16 h to optimize for IL-13 secretion. In this instance, only ionomycin induced detectable levels of IL-3 in cultures stimulated for either 4 h (457 ± 27 pg/10⁶ basophils) or 24 h (4844 ± 2784 pg/10⁶ basophils) in the presence of IL-3R Ab.

**FIGURE 6.** CD69 expression is induced on basophils following IgE-dependent secretion and is mediated by autocrine IL-3. A. Kinetics for CD69 expression on basophils following stimulation with anti-IgE (10 ng/ml) using cells from three different subjects. Numbers within parentheses indicate the percentage histamine released at the 1 h time point. B. Basophils from eight different subjects were stimulated as indicated in the presence of IL-3R Ab or isotype control (both at 2 μg/ml). Basophils were then fixed after 4 h of incubation and stained for CD69. C. Control cultures showing that IL-3R Ab inhibits CD69 expression on basophils stimulated for 4 h with IL-3 (5 ng/ml).

>1000-fold above those seen with cells cultured in medium alone (n = 3).

Generally reported on basophils during short-term (i.e., 30 min) activation, we did see increases in CD69 expression on basophils stimulated for ≥1 h, with levels peaking between 2 and 4 h and remaining elevated for up to 24 h poststimulation (Fig. 6A). The intensity of this response was seemingly dependent on the concurrent histamine release response (percentage release in parentheses) following anti-IgE stimulation. Since this time course coincides with IL-3 generation, we sought to determine the contribution of this cytokine by attempting to block CD69 induction with anti-IL-3R Ab. As shown in Fig. 6B, the up-regulation of CD69 expression on basophils stimulated with anti-IgE (after 4 and 16 h)
was significantly inhibited (−35%) with the addition of anti-IL-3R Ab, relative to isotype controls (p < 0.003, n = 7). Although not shown, the histamine released in the 4-h cultures was unaffected with neutralization of IL-3. As expected, the CD69 induced on basophils in control cultures treated with recombinant IL-3 (5 ng/ml) was also suppressed (−66%) with the addition of the IL-3R Ab (p < 0.009, n = 6).

The evidence that autocrine IL-3 activity was indeed responsible for CD69 induction was further supported by results from an experiment where basophils were cultured at different densities (i.e., 2, 0.4, and 0.08 × 10⁷/ml) for 16 h with and without anti-IgE. CD69 levels were not induced on basophils cultured at these densities in medium alone (normalized MFI = 0.20, 0.10, and 0.14, respectively) but were when activated by anti-IgE (normalized MFI = 145.63, 137.32, and 93.06, respectively). Overall, the levels induced were quite comparable and did not reflect differences (up to 25-fold) in cell densities, as would be predicted if CD69 induction was due solely to paracrine IL-3 activity.

Discussion
Overall, the data presented herein indicate that human basophils generate IL-3 with parameters identical to those described for their production of IL-4 (11, 12). In particular, increases in IL-3 mRNA were seen as early as 15 min following stimulation with anti-IgE Ab, with evidence of IL-3 secretion within the first hour and peaking by 4 h after activation. Of course, the rapid secretion of IL-3 only became apparent after blocking its absorption using IL-3R Ab (Fig. 2). It therefore is reasoned that the rapid production of IL-3 plays an important role in allowing for autocrine priming for subsequent effector functions (as discussed below). Another feature of IL-3 production by basophils that bears remarkable similarity to that of IL-4 is its strong link to IgE/FcεRI-dependent activation. Basophils responding well to anti-IgE stimulation (with regard to histamine release) up-regulated IL-3 mRNA by as much as several thousand-fold after 1 h and were also more likely to secrete protein for this cytokine (Figs. 1 and 3). In contrast, common basophil secretagogues such as C5a, FMLP, and PMA that are all quite potent at degranulating (1) mast cells used in these studies were in fact first exposed to exogenously added IL-3 to induce their development from precursor cells. It therefore seems possible that this added IL-3 may have played a role in regulating its own production. Moreover, unlike the mouse data, which implicated the importance of IL-3 in mast cell development and function, recent evidence indicates that IL-3 does not affect the differentiation of human mast cells (15). Thus, these issues raise questions regarding the translatability of the two models, particularly pertaining to the role of IL-3 in mast cell vs basophil function.

Nonetheless, the results presented in the present study are not unlike those seen with murine mast cells in that they clearly show that human basophils also rapidly generate mRNA and secrete protein for IL-3 within the first 4 h following IgE-dependent activation. However, the basophil studies are clearly more relevant to clinical disease in demonstrating that they utilize the IL-3 they produced. For example, in vitro studies have long shown IL-3 to be the most potent cytokine to affect human basophil function, and that it does so by binding receptors densely expressed on their cell surface. It is therefore plausible that these cells may very well regulate their own priming in vivo. The importance of this hypothesis is underscored by the long-standing idea that in vitro basophil releasability is clinically relevant (16). In fact, many studies conducted during the past 30 years have shown evidence that basophils from allergic subjects are primed both functionally and phenotypically when compared with cells from normal subjects.

To investigate the possibility that basophils mediate their own priming, we explored whether the IL-13 generated by these cells following IgE-dependent activation is indeed secondary to IL-3 secretion. It seemed possible that the prolonged kinetics (~24 h) originally reported for optimal IL-13 secretion (17) vs the time course for IL-4 (~4 h) (12) in response to IgE-dependent activation are actually due to the actions of autocrine IL-3. By neutralizing IL-3 activity using IL-3R Ab, we were able to demonstrate that ~30% of the IL-13 secreted during a 16-h incubation was dependent on autocrine activity (Fig. 5). Of note, we accurately predicted that neutralizing IL-3 would have less of an effect on IL-4 (~19% reduction) and histamine (no change), since release of these mediators, respectively, occurs either simultaneously or before IL-3 is produced. However, it is also fair to conclude that much of the IL-13 produced during IgE-dependent activation is in fact independent of IL-3. This finding thus supports our long-held idea that at least two pathways exist in basophils for the production of IL-13: one that is FcεRI-mediated, and one that is dependent on IL-3 (1). Therefore, the IL-3 produced by basophils likely functions, in part, to augment and/or prolong the secretion of IL-13 that is initiated upon IgE-dependent activation.
Evidence that basophils might mediate their own priming is also supported by the finding that autocrine IL-3 induces the expression of CD69 following IgE-dependent activation. First, note that Suzukiwa et al. have recently shown that low-level FceRI-dependent activation up-regulates CD69 expression on basophils, but only under conditions that involve the addition of IL-3 along with the anti-FceRI Ab used in these studies (18). Our results confirm that basophils express CD69 following IgE-dependent activation, but they additionally show that IL-3 does not need to be added exogenously to do so (Fig. 6A). In observing the relatively slower kinetics for CD69 induction (≥1 h) compared with the minutes for the up-regulation of degradation-specific markers (i.e., CD63 and CD203c), we then hypothesized that the former is regulated indirectly by autocrine IL-3. Indeed, this was our conclusion after confirming that the addition of IL-3 Ab markedly inhibited CD69 induction resulting from IgE-dependent activation (Fig. 6, B and C).

Overall, these in vitro findings demonstrating that autocrine IL-3 modulates basophil IL-13 secretion and CD69 expression could help interpret clinical observations. Several studies have shown that basophils produce IL-13 in direct response to IL-3 (3, 4) and that this reaction is greater using cells from allergic vs normal controls (19). Circulating basophils have also been shown to spontaneously secrete IL-13 following experimental allergen challenge in the nose compared with prechallenge responses (20). Likewise, Yoshimura et al. first reported constitutive expression of CD69 on the basophils of asthatics compared with normal subjects (21). This has since been extended to include basophils prepared from allergic rhinitics and subjects with chronic idiopathic urticaria (22). We have also shown that circulating basophils from subjects allergic to insect venom express greater levels of CD69 following a controlled insect sting compared with pre-sting levels (23). Therefore, it seems feasible that the basophils from these subjects are primed for greater IL-13 secretion and expression of CD69 having come in contact with IL-3. More significantly, the data strongly and preferentially induced by IL-3. A. F. Walls, C. Ra, T. Iwata, et al. 2002. Activation markers of human basophils: role of low-level stimulation.

In conclusion, we have shown that human basophils rapidly generate and secrete IL-3 upon IgE-dependent stimulation. Through autocrine activity, this IL-3 is capable of priming basophils for functional and phenotypic properties characteristic of basophils isolated from allergic individuals. We predict that autocrine IL-3 activity resulting from low-level IgE/FceRI cross-linking by specific allergen represents an important mechanism behind the hyperreactive nature of basophils that has long been observed in allergic disease.

Disclosures

The authors have no financial conflicts of interest.

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