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Overproduction of IgE Induces Macrophage-Derived Chemokine (CCL22) Secretion from Basophils

Maki Watanabe,1* Takahiro Satoh,1,2* Yoshihiro Yamamoto,*, Yasumasa Kanai,** Hajime Karasuyama,† and Hiroo Yokozeki*

Macrophage-derived chemokine (MDC) CCL22 is a potent chemoattractant for Th2 cells and has been implicated in Th2-predominant allergic inflammation. In the present study, we demonstrated that basophils produce MDC in response to monomeric IgE. In trinitrophenyl (TNP)-IgE transgenic mice, serum levels of MDC were persistently higher than in wild-type mice. The iv. administration of TNP-specific IgE to wild-type mice transiently induced an elevation in serum MDC, which appeared to be mediated by FcεRI, as no increase in serum MDC was observed after IgE administration in FcεRI (−/−) mice. However, the IgE-mediated increase in MDC was observed in mast cell-deficient mice. Freshly isolated bone marrow cells and bone marrow-derived basophils secreted MDC in response to TNP-IgE without Ag stimulation. Furthermore, MDC production was not observed in bone marrow-derived basophils isolated from FcεRI (−/−) mice. IgE activated Lyn and ERK 1/2 in bone marrow-derived basophils. Treatment of TNP-IgE transgenic mice with a basophil-depletion Ab (Ba103) resulted in decreased serum MDC levels. Thus, IgE appears to be capable of stimulating basophils to produce MDC in the absence of a specific Ag, which may contribute to IgE-mediated and/or Th2-predominant allergic inflammation. The Journal of Immunology, 2008, 181: 5653–5659.

In recent years, a considerable amount of attention has been paid to the roles of chemokines that attract effector cells in inflammatory responses. Macrophage-derived chemokine (MDC) CCL22 is a C-C chemokine secreted by a variety of cells, such as macrophages, monocytes, dendritic cells, and B cells (1, 2). MDC acts as a chemoattractant for CCR4-expressing cells (3, 4), including Th2-type lymphocytes, and it has been implicated in allergic diseases. MDC production is increased in asthmatic patients (5, 6), and the blocking of MDC causes an impaired reaction in asthmatic models in mice (7). Serum levels of MDC are increased and correlated with skin disease activity in patients with atopic dermatitis (8, 9). However, the mechanisms leading to the persistent production of MDC in allergic diseases are not fully understood.

Chronic allergic skin diseases, such as atopic dermatitis, are frequently accompanied by increased levels of serum IgE. IgE is thought to evoke skin inflammation via the activation of mast cells. Mast cells degranulate a variety of chemical mediators, including histamines and prostaglandins, by the interaction of IgE and Ag, resulting in the immediate-type reactions (ITR), such as the wheal-and-flare skin response. The late-phase responses (LPR) occur hours after the ITR. The LPR is histologically characterized by a dermal cellular infiltrate comprised of lymphocytes, neutrophils, and eosinophils. The LPR is also a mast cell-dependent reaction that is probably initiated by mast cell-derived cytokines, such as TNF-α and IL-4 (10), and possibly by several chemokines; the cytokines stimulate the expression of cell adhesion molecules on dermal endothelial cells, and the chemokines mediate the chemotraction of effector cells. A recent study demonstrated that transgenic mice overexpressing IgE exhibited a strong “third-phase reaction” following the ITR and LPR (11, 12). This third-phase reaction lasts for several days and is histologically characterized by a dense cellular infiltrate comprised of lymphocytes and eosinophils with epidermal hyperplasia and hyperkeratosis (11), which indicate a chronic allergic inflammation. In addition, the striking finding was that basophils, but not mast cells, were essential for the development of the IgE-mediated third-phase reaction (12). These findings unveiled novel and overlooked pathological roles of IgE and basophils in chronic allergic inflammation.

Both basophils and mast cells express the αβγ2 form of FcεRI; the α-chain is responsible for binding the Fc portion of IgE, whereas the β- and γ-chains contain the tyrosine-based activation motifs responsible for transducing the activation signal in the cells (13, 14). The traditional understanding of cell activation via FcεRI has been that IgE binds to FcεRI, resulting in cell priming and the increased surface density of FcεRI; but IgE binding does not evoke the activation events, such as the release of preformed granule-associated mediators, newly synthesized arachidonic acid metabolites, and cytokines. The full activation of FcεRI requires cross-linking of the α-chain, which is mediated by binding to multivalent allergen through surface IgE. Nevertheless, recent studies with mast cells revealed that monomeric IgE in the absence of a specific Ag can activate several signaling events, leading to prolonged cell survival, degranulation, and the production of cytokines such as IL-6 and
TNF-α (15–22). These observations have changed the conceptual understanding of IgE binding to cells from a pre-activating event to a full-activating event. Thus, it is conceivable that high levels of IgE may persistently stimulate mast cells and/or basophils to release inflammatory mediators before exposure to allergens and may modify or reinforce the subsequent allergic reactions evoked by allergen challenge. However, not all monoclonal IgE molecules induce complete cell activation. IgEs display heterogeneity in that different IgE molecules induce varied levels of activation. Highly cytokinergic IgEs induce cytokine secretion and other activation events including degranulation, whereas other IgEs do not efficiently lead to these events (16, 17, 19, 20).

In the present study, we found that mice overexpressing trinitrophenyl (TNP)-specific IgE have unique properties characterized by a higher production of MDC than in wild-type mice. We attempted to elucidate the mechanisms of MDC generation and demonstrated that basophils seem to be persistently generating MDC by the binding of TNP-IgE to FcεRI on their surface in the absence of an Ag.

Materials and Methods

Mice

BALB/c, C57BL/6, C3H/HeJ, and WBB6F1-Sld mice were purchased from Sankyo Labo Service. FcεR-chain−/− C57BL/6 mice (23) were purchased from The Jackson Laboratory. TNP-specific IgE transgenic mice were described previously (24). Mice were maintained under specific pathogen-free conditions in our animal facility. The use of animals was in full compliance with the Committee for Animal Experiments of Tokyo Medical and Dental University.

Preparation of monomeric IgE

TNP-specific IgE was derived from the FGEI b4 B cell hybridoma (American Type Culture Collection) by collecting in vitro culture supernatants. In some experiments, IgE was obtained from ascites of CD1 (ICR)nu/nu mice by i.p. injection of the hybridoma. Supernatants were subjected to precipitation with 50% saturated ammonium sulfate and dialysis in PBS. Dinitrophenyl (DNP)-specific IgE (SPE-7) was obtained from Sigma-Aldrich (Sigma-Aldrich) dissolved in 0.1 M citrate buffer (pH 5.0) in a 96-well microtiter plate at 37°C for 1.5 h. The reaction was stopped with 20 µl/well of 0.1 M carbonate buffer (pH 10.5). The plate was read at 405 nm in an ELISA reader. The net percentage of β-hexosaminidase release was calculated as follows: (β-hexosaminidase in supernatants)/(β-hexosaminidase in supernatant + β-hexosaminidase in pellet) × 100 (%).

Real-Time PCR

Total cellular RNA was isolated by using Isogen (Nippon Gene). Twenty microliters of reverse transcription mix consisted of 8 µl of 5 × buffer (250 mM Tris-HCl, pH 8.3, 375 mM KCl, 10 mM HEPES, and 10 ng/ml IL-3). Cells were seeded at 5 × 105 cells/ml on a 24-well plate and incubated for 20 min at 37°C. They were stimulated with TNP-IgE or DNP-IgE for 30 min. At the end of the incubation period, the plate was transferred to ice, and the cells were centrifuged at 500 × g for 10 min at 4°C. After collection of the supernatant, the pellets were solubilized in the original volume of HEPES-Tyrode’s buffer containing 0.5% Triton-X 100. Next, 50 µl of sample (in duplicate) was incubated with 50 µl of 1 mM p-nitrophenyl-N-acetyl-β-n-glucosaminide (Sigma-Aldrich) dissolved in 0.1 M carbonate buffer (pH 9.4) in a 96-well microtiter plate at 37°C for 1.5 h. The reaction was stopped with 200 µl/well of 0.1 M carbonate buffer (pH 10.5). The plate was read at 405 nm in an ELISA reader. The net percentage of β-hexosaminidase released was calculated as follows:

\[
\text{Net percentage} = \frac{\text{β-hexosaminidase in supernatants}}{\text{β-hexosaminidase in supernatant} + \text{β-hexosaminidase in pellet}} \times 100\%.
\]

Measurement of MDC/CCL2

Serum was collected by centrifugation of blood obtained from the retro-orbital plexus. The concentration of MDC was measured with ELISA kits (R&D Systems).

Immunoblotting analysis

Cells stimulated with IgE and/or Ags were washed with ice-cold PBS (−) and lysed in 1% Triton-containing lysis buffer (20 mM Tris-HCl (pH 7.5), 150 mM NaCl, 1 mM EDTA, 2.5 mM sodium pyrophosphate, 1 mM β-glycerocephosphate, 1 mM Na3VO4, 1 µg/ml leupeptin, and 1 mM PMSF). Cell lysates were analyzed by SDS-PAGE followed by immunoblotting. Proteins reactive with primary Abs, such as anti-phospho Src family Ab (Tyr416) (Cell Signaling Technology), anti-Lyn Ab (Santa Cruz Biotechnology), anti-phospho-p42/44 MAPK Ab (Th2/Th2/Th20; Cell Signaling Technology), and anti-phospho p44/42 MAPK Ab (Cell Signaling Technology), anti-phospho p44/42 MAPK Ab (Cell Signaling Technology) were detected using the methods described previously (26). In brief, bone marrow cells were aspirated from 6- to 8-wk-old mice, and Lin−/- bone marrow progenitor cells were isolated with Spin Sep Ab mixture (StemCell Technologies). These cells were cultured with rIL-3 (Wako Pure Chemical Industries, Ltd.; 10 ng/ml) for 10 days. The c-kit−/- basophil-like cells were obtained by negative selection with biotin-conjugated anti-mouse c-kit Ab (eBioscience) and streptavidin microbeads (Millen Biotech) by using magnetic cell sorting. FcεRI+/c-kit−/- cells constituted ∼70−80% of these cell suspensions as assessed by flow cytometry (data not shown).

Bone marrow-derived mast cells (BMMC) were prepared by culturing bone marrow cells in RPMI 1640 medium that contained 10% FCS, 10 mM nonessential amino acids, 10 mM sodium pyruvate, 25 mM HEPES buffer, 50 µM 2-ME, and rIL-3 (250 µg/ml) for 5 wk. More than 98% of BMMC were positive for FcεRI and c-kit−, as assessed by flow cytometric analysis with FITC-labeled anti-mouse FcεRI Ab (MAR-1; eBioscience) and PE-labeled anti-c-kit Ab (BD Biosciences).

Peritoneal mast cells were prepared as described previously (27, 28) with some modifications. Briefly, mice were injected i.p. with 5 ml of RPMI 1640. The peritoneal lavages were collected after gentle massages of the orbital plexus. The concentration of MDC was measured with ELISA kits (R&D Systems).

Stimulation of cells with monomeric IgE

BMMa or BMMC (5 × 105 cells/ml) were incubated for 24 h with the indicated concentrations of IgE in RPMI 1640 that contained 10% FCS. Supernatants were collected and stored at −20°C until use.

Preparation of TNP-OVA

OVA (Sigma-Aldrich; 50 mg/1.5 ml) was mixed with 2.5 ml of 0.1 M Na2BO3 buffer (pH 9.3) and incubated with 1 ml of 5% 2,4,6-trinitrobenzenesulfonic acid (Nacalai Tesque) and 10 µl of 1 M Na2CO3 overnight at room temperature. OVA conjugated with more than 11 molecules of TNP per protein was used for the experiments after dialysis with PBS (11, 12).

Stimulation of cells with Ags

Cells were primed overnight with 0.5 µg/ml TNP-IgE or 0.5 µg/ml DNP-IgE, then washed and stimulated with 20 ng/ml TNP-OVA or DNP-HSA (Sigma-Aldrich) for 24 h. Supernatants were collected and stored at −20°C until use.

Degranulation assay

Degranulation was assessed by using a previously reported method to measure the release of β-hexosaminidase (29, 30). Cells were washed with Tyrode’s salt solution (pH 7.4) containing 0.04% BSA, 10 mM HEPES, and 10 ng/ml IL-3. Cells were seeded at 5 × 105 cells/ml on a 24-well plate and incubated for 20 min at 37°C. They were stimulated with TNP-IgE or DNP-IgE for 30 min. At the end of the incubation period, the plate was transferred to ice, and the cells were centrifuged at 500 × g for 10 min at 4°C. After collection of the supernatant, the pellets were solubilized in the original volume of HEPES-Tyrode’s buffer containing 0.5% Triton-X 100. Next, 50 µl of sample (in duplicate) was incubated with 50 µl of 1 mM p-nitrophenyl-N-acetyl-β-n-glucosaminide (Sigma-Aldrich) dissolved in 0.1 M citrate buffer (pH 5.0) in a 96-well microtiter plate at 37°C for 1.5 h. The reaction was stopped with 200 µl/well of 0.1 M carbonate buffer (pH 10.5). The plate was read at 405 nm in an ELISA reader. The net percentage of β-hexosaminidase released was calculated as follows: (β-hexosaminidase in supernatants)/(β-hexosaminidase in supernatant + β-hexosaminidase in pellet) × 100 (%).
were visualized with an HRP-conjugated secondary Ab and ECL reagents (Amersham Biosciences).

Statistical analyses

The Student’s t test was used to assess the statistical significance of differences between mean values. Values of \( p < 0.05 \) were considered statistically significant.

Results

TNP-IgE induces serum MDC production in vivo

Fig. 1A shows MDC levels in TNP-specific IgE transgenic mice. Serum levels of MDC in TNP-IgE transgenic mice were persistently higher than those in wild-type BALB/c mice. To examine the mechanisms of increased MDC production in TNP-IgE transgenic mice, we i.v. administered TNP-IgE (300 µg/mouse) into wild-type BALB/c mice. IgE was prepared from hybridoma IGEL b4, because TNP-IgE transgenic mice carry the genes that encode the heavy and light chains of IGEL b4, an anti-TNP-IgE-producing hybridoma (24). The i.v. administration of TNP-IgE caused increased MDC levels (Fig. 1B). MDC production reached a peak level at 24–30 h after IgE injection and returned to a basal level after 48 h (data not shown). TNP-IgE-induced MDC production was almost completely abrogated in FcR\( \gamma \) (−/−) mice, but not in wild-type C57BL/6 mice (Fig. 1B). FcR\( \gamma \) (−/−) mice lack not only the IgE receptor, but also the IgG receptor. However, it was unlikely that MDC production was mediated by the IgG receptor. The administration of control IgG (MOPC-31c; Sigma-Aldrich) into BALB/c mice did not result in the increased MDC levels (data not shown). Therefore, these data suggest that IgE stimulates MDC synthesis through the Fc\( \gamma \)R1 receptor. The contamination of endotoxin in prepared IgE samples was less than 0.005 EU/ml (Endospecy ES-50M kit; Seikagaku). Moreover, the increase in serum MDC levels by IgE injection was also observed even in TLR4-mutant C3H/HeJ mice (238.6 ± 18.39 pg/ml vs 331.2 ± 28.4 pg/ml, control and TNP-IgE-injected mice, respectively, \( p < 0.05 \)).

MDC production in mast cell-deficient mice

Because mast cells constitute a major population of Fc\( \gamma \)RI-expressing cells in mice, we postulated that mast cells could be a source of MDC and that TNP-IgE-induced MDC production would be abrogated in mast cell-deficient mice. Unexpectedly, however, the serum levels of MDC were weakly but significantly increased after TNP-IgE injection in mast cell-deficient WBB6F1-Sl/Sld mice (Fig. 1C). Thus, cells other than mast cells were secreting MDC in response to IgE.

MDC production from bone marrow cells

To further explore the source of MDC, we examined MDC production from bone marrow cells. Freshly isolated bone marrow cells from BALB/c mice were incubated with monomeric
TNP-IgE for 24 h. MDC was secreted when these cells were stimulated with IgE for 24 h induced a small but significant increase in MDC mRNA synthesis as assessed by real-time PCR analysis. FNC-IgE were primed with TNP-IgE (0.5 μg/ml) or DNP-IgE (0.5 μg/ml) overnight, followed by stimulation with 20 ng/ml TNP-OVA or DNP-HSA. Results representative of three separate experiments are shown. * p < 0.05.

**FIGURE 3.** MDC production from basophils. A, BMBa were prepared as described in Materials and Methods. These cells expressed FceRI but not c-kit. Dotted lines indicate negative control staining. B, BMBa secreted a large amount of MDC in response to IgE. DNP-IgE appeared to be more potent than TNP-IgE. C, Deficiency of the Fcγ-receptor resulted in the complete abrogation of MDC production from BMBa. D, OVA-IgG (5 μg/ml) was not capable of inducing MDC production in BMBa from BALB/c mice. E, Stimulation of BMBa with IgE for 24 h induced a small but significant increase in MDC mRNA synthesis as assessed by real-time PCR analysis. F, BMBa were primed with TNP-IgE (0.5 μg/ml) or DNP-IgE (0.5 μg/ml) overnight, followed by stimulation with 20 ng/ml TNP-OVA or DNP-HSA. Results representative of three separate experiments are shown. * p < 0.05.

**Basophils produce MDC in response to IgE**

Prior evidence indicates that bone marrow does not contain mature mast cells that express FceRI (31). Consistent with this evidence, we were unable to detect FceRI (+)/c-kit (+) mast cells in freshly isolated bone marrow cells. There were FcεRI (+)/c-kit (+) cells that constituted less than 2% of bone marrow cells in BALB/c mice and even in mast cell-deficient WBB6F1-Sld/Sld mice (data not shown). Thus, we postulated that MDC secreted from fresh bone marrow cells was derived from another type of FcεRI-expressing cell, i.e., basophils.

Next, we prepared basophils by culturing Lin (−) bone marrow progenitor cells maintained with IL-3 for 8–10 days followed by the depletion of c-kit (−) cells (Fig. 3A). As expected, BMBa produced a significant amount of MDC when stimulated with IgE (Fig. 3B). An almost complete abrogation of MDC release was observed in FcεRI−/−-derived BMBa (Fig. 3C). Moreover, OVA-specific IgG was not capable of stimulating BMBa of BALB/c mice to secrete MDC (Fig. 3D), again confirming the involvement of FcεRI but not IgG receptors.

Unstimulated BMBa expressed MDC mRNA (data not shown). In addition, IgE stimulation resulted in enhanced MDC mRNA synthesis as assessed by real-time PCR analysis (Fig. 3E). The increase in the level of MDC mRNA was detected at 6 h (data not shown) and peaked at 24 h for DNP-IgE, whereas TNP-IgE-induced mRNA synthesis had a small but statistically significant increase that was detected only at 24 h.

**Comparison of MDC production from BMBa between IgE and IgE+Ag**

The capability of BMBa to secrete MDC via signaling through FcεRI was further confirmed by the remarkable MDC generation...
that occurred when BMBa were stimulated with IgE plus the corresponding Ags. Notably, the activation abilities of TNP- and DNP-IgEs were similar when stimulated together with Ags (Fig. 3F), while TNP-IgE alone appeared to be less cytokinergic than DNP-IgE alone (Fig. 3B).

FcεRI-mediated signaling in mast cells includes several activation events, such as the activation of Lyn, Syk, Btk, and MAPKs (16, 19, 22). In BMBa, both TNP- and DNP-IgE induced phosphorylation of Lyn and ERK 1/2 (Fig. 4A). Similarly, IgE+Ag activated these signals in a manner that was faster and/or stronger than the signals induced by IgE alone (Fig. 4B).

**MDC secretion from mast cells**

We next tested whether mast cells were capable of producing MDC in vitro. BMMC were stimulated with TNP- or DNP-IgE. As shown in Fig. 5A, DNP-IgE stimulated mast cells to produce MDC, but the protein levels were much lower than those of BMBa (Fig. 3B), and the MDC secretion induced by TNP-IgE was undetectable. Despite the low capability of MDC production by IgE, BMMC treated with IgE exhibited significant degranulation as assessed by the β-hexosaminidase assay (31.8 ± 2.72% vs 3.4 ± 0.49% for TNP-IgE and negative control, respectively). Both TNP- and DNP-IgE induced MDC secretion from BMMC when they were stimulated together with their corresponding Ags (Fig. 5B). However, the amount of MDC secreted by BMMC was much less than the amount of MDC secreted by BMBa (Fig. 3F).

**Depletion of basophils reduces serum MDC in vivo**

To confirm that basophils secreted MDC in vivo, basophil depletion Ab (Ba103) (32) or control rat IgG (Sigma-Aldrich) was i.v. injected into IgE transgenic mice (30 μg/mouse), and serum levels of MDC before and after Ab treatment were measured. As expected, the serum levels of MDC decreased after basophil depletion (Fig. 6). The effect was most marked at 4 days after injection and gradually returned to the basal level within two weeks (data not shown). MDC production from basophils in vivo was further confirmed by the results that wild-type BALB/c mice pretreated with Ba103 Ab 4 days before TNP-IgE injection did not exhibit inducible synthesis of serum MDC (data not shown).

**Discussion**

The TNP-IgE transgenic mice, which were generated by transgenes from a TNP-specific IgE-producing hybridoma (IGEL b4), have persistently high levels of IgE in their sera (19–22). These mice show no significant abnormalities at birth or during postnatal growth. However, the peritoneal mast cells in IgE transgenic mice express 6 to 8 times higher amounts of FcεRI on their surface than do the peritoneal mast cells from their nontransgenic littermates (24). This is probably due to the IgE-mediated inhibition of FcεRI internalization (33). In the present study, we observed another unique phenotype of TNP-IgE transgenic mice; we found that the serum levels of MDC are persistently higher in the transgenic mice than in wild-type mice. It is likely that the increased level of MDC was mediated by IgE, because the administration of TNP-IgE (IGEL b4) into wild-type mice induced a transient increase in the level of MDC. We identified basophils, but not mast cells, as a major source of IgE-induced MDC.

Recent evidence has revealed that IgE bind to FcεRI results in degranulation and cytokine production without Ag stimulation in mast cells (15–22). In vitro analyses in the present study revealed that BMBa produce a significant amount of MDC in response to IgE in the absence of a specific Ag. This is the first study to demonstrate that monomeric IgE is capable of stimulating basophils to secrete MDC. It was also revealed that TNP-IgE (IGEL b4) is a cytokinergic IgE, although SPE-7 (DNP-IgE) appeared to be more cytokinergic than TNP-IgE.

The precise mechanisms of basophil activation by monomeric IgE have not yet been fully elucidated. However, in studies with mast cells, highly cytokinergic IgEs can induce small clusters of FcεRI aggregates in lipid drafts by reducing repulsion between neighboring FcεRI molecules. This clustering seems to be mediated by interaction between hypervariable regions of IgE molecules (22), as monovalent hapten can inhibit IgE-induced cell activation (17). Thus, signals mediated by IgE alone are basically the same as signals mediated by IgE+Ag in mast cells. In the present study with BMBa, we observed the similarity in the signaling events, such as Lyn and ERK in IgE-induced stimulation vs IgE+Ag-induced stimulation. In addition, intracellular signals triggered by IgE without Ag were weak and slow compared with those triggered by IgE+Ag, as observed in the prior studies of mast cells (19, 22).

It was interesting that the high production of MDC was sustained in the TNP-IgE transgenic mice, while a single exposure of wild-type mice to TNP-IgE induced a transient MDC generation that peaked 24 to 28 h after injection and returned to a basal level after 48 h. Weak signals induced by monomeric IgE might enable blood basophils to continuously synthesize MDC.
in vivo, probably in collaboration with increased surface expression of FceRI (33) and/or prolonged cell survival (17), which are also sustained by IgE binding to its receptors. Alternatively, IgE may also bind to premature bone marrow basophils, which are constitutively generated in the bone marrow, and this binding may result in the persistently increased serum levels of MDC.

In contrast to the remarkable production of MDC by BMBa, BMMC secreted lower amounts of MDC (Fig. 5). Data (not shown) also demonstrated that peritoneal mast cells were even less potent than BMMC in secreting MDC. The underlying mechanisms that are responsible for the extremely different capabilities for MDC production between basophils and mast cells are unclear. We found that c-kit(−) basophils and c-kit(+) cells appearing in vitro culture of bone marrow cells with IL-3 for 8 days secreted similar amounts of MDC when stimulated with IgE (data not shown), while c-kit(+) mature mast cells cultured for 5 wk did not efficiently secrete MDC. It seemed that bone marrow progenitor cells gradually lost their capability for MDC production during the long-term culture with IL-3. Mast cells might preserve enough ability to produce MDC before completing their maturation. Similarly, basophils in the bone marrow may be more potent than mature basophils in the peripheral blood in regard to their MDC-producing capability. It will be interesting to determine the different capabilities for MDC production in different cell lineages and maturation stages.

The enhancement in serum MDC levels of mast cell-deficient WBB6F1/SJLd mice was not marked compared with wild-type C57BL/6 mice (Fig. 2, B and C), although the increase was statistically significant. A high number of mast cells reside in the skin, gut, respiratory tract, and other organs, as compared with the number of basophils, which constitute a minimal population in skin, gut, respiratory tract, and other organs, as compared with the number of basophils, which constitute a minimal population in

Collectively, the present data reveal that overproduction of IgE-induced MDC release from basophils. MDC from basophils may contribute to allergic inflammation, a condition in which IgE is persistently increased.

Disclosures

The authors have no financial conflict of interest.

References


