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An Increase in Circulating Mast Cell Colony-Forming Cells in Asthma

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and Atsushi Komiyama*‡

We compared a potential to generate mast cells among various sources of CD34+ peripheral blood (PB) cells in the presence of stem cell factor (SCF) with or without thrombopoietin (TPO), using a serum-deprived liquid culture system. From the time course of relative numbers of tryptase-positive and chymase-positive cells in the cultured cells grown by CD34+ PB cells of nonasthmatic healthy individuals treated with G-CSF, TPO appears to potentiate the SCF-dependent growth of mast cells without influencing the differentiation into mast cell lineage. CD34+ PB cells from asthmatic patients in a stable condition generated significantly more mast cells under stimulation with SCF alone or SCF+TPO at 6 wk of culture than did steady-state CD34+ PB cells of normal controls. Single-cell culture studies showed a substantial difference in the number of SCF-responsive or SCF+TPO-responsive mast cell progenitors in CD34+ PB cells between the two groups. In the presence of TPO, CD34+ PB cells from asthmatic children could respond to a suboptimal concentration of SCF to a greater extent, compared with the values obtained by those of normal controls. Six-week cultured mast cells of asthmatic subjects had maturation properties (intracellular histamine content and tryptase/chymase enzymatic activities) similar to those derived from mobilized CD34+ PB cells of nonasthmatic subjects. An increase in a potential of circulating hemopoietic progenitors to differentiate into mast cell lineage may contribute to the recruitment of mast cells toward sites of asthmatic mucosal inflammation.

Asthma is an inflammatory disease, characterized by the infiltration of eosinophils, neutrophils, basophils, and lymphocytes in the airway wall and the surrounding parenchyma. Recently, it is proposed that hemopoietic myeloid progenitors contribute to the ongoing recruitment of inflammatory cells such as eosinophils to sites of allergen challenge in this disorder (1–5). It is well known that this inflammatory process is caused by mast cell activation through cross-linking of the high affinity IgE receptor (FcεRI). Mast cells originate from pluripotent hemopoietic cells within the marrow. Mast cell progenitors depart from the bone marrow (BM)1 and migrate into the connective or mucous tissues, where they differentiate into the mature form. In the human system, mast cell progenitors are positive for CD34, c-kit, CD13, and CD38, but lack HLA-DR (6–9). Stem cell factor (SCF) has been reported to act as a major growth and differentiation factor for the human mast cell development from cord blood mononuclear cells (10), BM cells (11, 12), and fetal liver cells (13). In contrast, our recent study showed that the addition of thrombopoietin (TPO) to culture containing SCF is a requisite for the significant production of mast cells from CD34+ BM cells (14).

It is demonstrated that PBMCs or CD34+ cells generate mast cells in the presence of SCF without or with IL-3 (7, 12). In addition, Rottem et al. (7) reported that the number of mast cells arising per CD34+ cell is greater in patients with aggressive mastocytosis than normal subjects. However, little is known about the kinetics of mast cell progenitors in allergic disorders. In this study, we compared the production of mast cells from CD34+ peripheral blood (PB) cells between asthmatic patients and normal controls, using a serum-deprived culture system.

Materials and Methods

Subjects

Six normal donors for allogeneic PB stem cell transplantation aged 7.5 ± 4.7 (range, 3–15) years were enrolled in this study. They had no known diseases including allergic disorders, and took no medications. All donors and/or their parents provided written informed consent. Donors received G-CSF (Chugai Pharmaceutical, Tokyo, Japan) s.c. at a dose of 10 μg/kg for 5 consecutive days, and blood sampling was performed on day 5. The protocol was approved by the ethics committee of Shinshu University School of Medicine.

PB samples (10 ml) were harvested by venous puncture from a total of 10 males and three females with bronchial asthma aged 6.5 ± 4.0 (2–15) years after obtaining the fully informed consent of each patient and/or the parents. The asthma was defined according to the criteria of the American Thoracic Society. Twelve aged-matched healthy subjects and three nonallergic patients with lower respiratory tract infection were used as the control group. Based on the guidelines for the diagnosis and management of

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3 Abbreviations used in this paper: BM, bone marrow; PB, peripheral blood; SCF, stem cell factor; TPO, thrombopoietin; GPA, glycoprophorin A.
with atopic dermatitis, and from a 6-year-old boy with allergic rhinitis after (256–4711 IU/ml). All of the patients had positive immediate skin reac-
90% N 2 . Half of the culture medium was replaced weekly with fresh me-
a

The mean PB eosinophil count was 0.83

6

6

1– 4

After treatment with Silica (Immuno-Biological Laboratories, Fujioka, Ja-

CD13 (Immu103.44, PE-cyanin 5.1) was obtained from Immunotech.

FITC-conjugated anti-CD34 mAb for 30 min at 4°C. As negative controls,

FITC-conjugated mouse IgG1 (Becton Dick-

and stained with May-Gru¨nwald-Giemsa or per-

m

oxidase. Reactions with mouse mAbs against tryptase, chymase, CD2,

Tryptase and chymase enzymatic activity were measured according to the

Histamine concentrations in the cell lysates obtained by the treatment of

by guest on April 16, 2017 http://www.jimmunol.org/ Downloaded from

Histamine enzymine immunosassay Kit (Immunotech). The detection limit was

1 nM. All assays were conducted in triplicate.

Tryptase and chymase enzymatic assay

Tryptase and chymase enzymatic activities were measured according to the procedure described by Xia et al. (20). The cultured cells (5 × 10^6) grown with SCF or SCF+TPO with 0.5 ml of 1% Triton X-100 containing 0.5 M KCl were measured with the His-

amine Enzyme Immunoassay Kit (Immunotech). The detection limit was 1 nM. All assays were conducted in triplicate.

Flow cytometric analysis

For the analysis of surface markers on CD34⁺ PB cells, 1–2 × 10⁶ PBMCs were incubated with 20 μl FITC-conjugated anti-CD34 mAb, 20 μl PE-conjugated anti-c-kit mAb, and 10 μl PC5-conjugated anti-CD13 mAb for 30 min at 4°C, as described previously (14). The cells were washed twice, after which their surface markers were analyzed with the FACScan flow cytometer, using the Lysis 2 software program. The lymphoblastic region was gated on the basis of their forward light and side scatter characteristics. Then, the second gate was set on CD34⁺ cells. The expressions of c-kit and CD13 on CD34⁺ cells were examined. The proportion of positive cells was determined by comparison to cells stained with FITC-, PE-, or PC5-conjugated mouse isotype-matched Ig.

Immunochemical staining

The cultured cells were spread on glass slides using a Cytospin II (Shandon Southern, Sewickly, PA) and stained with May-Grünwald-Giemsa or per-

reactions. Reactions with mouse mAbs against tryptase, chymase, CD2, CD11b, CD15, CD19, CD41, and GPA were detected using the alkaline phosphatase-anti-alkaline phosphatase (APAAP) method (Dako APAAP Kit System; Dako, Carpinteria, CA), as described previously (19). The isotype mouse mAb was also used as a control. Briefly, cytocentrifuged samples were fixed with Carnoy’s fluid, washed with PBS, and preincu-
bated with normal rabbit serum to saturate the Fc receptors on the cell surface. After being washed with PBS three times, the samples were re-
acted with each of the mouse mAbs for 30 min at room temperature in a humidified chamber. After three more washes with PBS, the samples were incubated with rabbit anti-mouse IgG Ab, washed three times, and succes-
vically reacted with the calf intestinal alkaline phosphatase-mouse mono-

clonal anti-alkaline phosphatase complex. Finally, alkaline phosphatase ac-
vivity was detected with naphthol AS-MX phosphatase, Fast Red TR, and

100 mM Tris (pH 9.0). The release of MCA was measured spectrofluoro-
meterically. As a control, we used MCA obtained from Peptide Institute. A total volume of 180 μl at 37°C for 1 h. The release of p-nitroanilide was determined spectrophotometrically. As a control, we used p-nitroanilide purchased from Sigma. The addition of PMSF (Nacalai Tesque) at 1 × 10^-3 M reduced the levels of tryptase enzymatic activity by 87.3%. For the assay of chymase enzymatic activity, aliquots of the samples (20 μl) were incubated with 0.2 mM succinyl-Ala-Ala-Pro-Phe-MCA (Peptide Institute, Osaka, Japan), 100 mM Tris (pH 7.8) containing 0.5 M KCl, and sonicated. Aliquots (20 μl) of the samples were incubated with 0.2 mM toryl-Gly-Pro-Lys-p-nitroanilide (Sigma), 50 mM HEPES (pH 7.6) containing 0.12 M NaCl, 100 μg/ml of a soybean trypsin inhibitor (Sigma), and 1 μg/ml of heparin sulfate proteoglycan (Sigma) in a total volume of 180 μl at 37°C for 1 h. The release of p-nitroanilide was determined spectrophotometrically. As a control, we used p-nitroanilide purchased from Sigma. The addition of PMSF (Nacalai Tesque) at 1 × 10^-3 M reduced the levels of chymase enzymatic activity by 87.3%.
We examined the effects of SCF (10 ng/ml), TPO (10 ng/ml), IL-3 as the mean counts of progeny are presented. Values are expressed of SCF, 10 ng/ml of TPO, 100 U/ml of IL-3, or 50 ng/ml of IL-6, alone or in combination. The number of viable cells was cultured in wells containing 2 ml of serum-deprived liquid cultures. Half of the culture medium was replaced weekly with fresh medium containing the factor(s). As presented in Fig. 1, SCF alone induced the production of significant numbers of progeny from CD34+ PB cells, with a peak of ~3 times the input quantity at 6 wk. The number of viable cells decreased at 8 wk. In the presence of TPO, IL-3, and IL-6 alone, the total cell number in a well estimated at 2 wk was 6400 ± 800, 3500 ± 900, and 1200 ± 200, respectively. Subsequently, the cell numbers were not measurable. The addition of IL-6 significantly reduced the number of progeny grown with SCF, consistent with the previous result (17). In the presence of SCF and IL-3, the total cell number was maintained from 2 to 6 wk. Two-thirds of 6-wk cultured cells reacted with anti-tryptase mAb, and some of the remaining cells were positive for peroxidase. In contrast, the addition of TPO caused a significant enhancement of the SCF-dependent cell generation from CD34+ PB cells. The number of viable cells reached maximal at 6 wk, and was 5- to 6-fold that at the beginning of the culture. There was a decline in the number of viable cells at 8 wk.

Under stimulation with SCF alone, ~70% of the cultured cells became positive for tryptase at 2 wk. A large portion of the cultured cells reacted with anti-tryptase mAb after 4 wk. Although the frequency of chymase+ cells was at a negligible or very low level at 2 wk, the percentage of the cells positive for chymase increased to ~80–90% at 4 wk. It is of interest that the relative numbers of both tryptase+ cells and chymase+ cells in the cultured cells generated by stimulation with SCF+TPO increased in parallel with the values in the cells grown with SCF alone during 8 wk. At 6 wk of the culture with SCF alone or SCF+TPO, the cells with other lineage-specific markers (CD2, CD19, CD11b, CD15, CD41, or GFA) were at negligible levels.

Asthmatic patients have more circulating hemopoietic progenitors with a potential to differentiate into mast cell lineage than normal controls

The combination of SCF and TPO was the most favorable stimulus for mast cell growth from CD34+ PB cells of asthmatic patients as well as from those mobilized with G-CSF. The numbers of tryptase+ cells grown at 4 wk by 1 × 10⁶ CD34+ PB cells were 20,700 ± 2,000 in SCF alone; 61,400 ± 9,000 in SCF+TPO; 17,700 ± 2,100 in SCF+IL-6; and 23,800 ± 3,100 in SCF+IL-3. Then, we compared the ability of CD34+ PB cells to generate mast cells between asthmatic children in a stable condition and controls. The results are presented in Fig. 2. CD34+ PB cells (2 × 10⁶) from healthy children generated 12,500 ± 6,300 cells at 6 wk of the culture with SCF+TPO. The numbers of the cultured cells from nonallergic patients with lower respiratory tract infection were 8300 ± 8100, being similar to the values obtained by healthy subjects. In contrast, CD34+ PB cells of asthmatic patients had a significantly higher potential to generate the progeny than did those of nonallergic controls (p < 0.01). A substantial difference was also observed in the culture containing SCF alone (84,000 ± 6,500 cells from 2 × 10⁶ CD34+ PB cells of three asthmatic children, and 3500 ± 1600 cells in three healthy subjects). Furthermore, in the presence of TPO, CD34+ PB cells from asthmatic children responded to a suboptimal concentration of SCF (1 ng/ml) to a greater extent than those from normal controls (Fig. 3). In both asthmatic individuals and nonallergic control subjects, >99% of 6-wk cultured cells were positive for tryptase, and >95% of them positive for chymase. However, an increase in the generation of mast cells from CD34+ PB cells was found in a part of patients with other allergic disorders (Fig. 2).

To elucidate why CD34+ PB cells from patients with asthma had the superior capability to yield mast cells, we compared the number of progenitors that gave rise to mast cell colonies by stimulation with SCF or SCF+TPO in CD34+ PB cells between the two groups, using single-cell cultures. The results are presented in Table I. In the presence of SCF+TPO, significantly greater numbers of colonies were formed in the cultures containing CD34+ PB cells from patients with asthma, as compared with the values obtained by normal controls. A prominent difference was also noted in the culture with SCF alone. A majority of the constituent cells of pooled colonies were positive for tryptase under stimulation with SCF alone or SCF+TPO in children with or without asthma. There was no significant difference in the size of mast cell colonies formed in the presence of SCF+TPO between asthmatic children and normal controls. The mean number of constituent cells in mast cell colonies was 70 ± 84 (20–312) in patient 1, 89 ± 129 (20–500) in patient 2, 28 ± 7 (23–48) in patient 3, 110 ± 258 (20–500).
from CD34 have been demonstrated that most of the human mast cells originate from three samples in each group. The results shown (mean ± SD) were derived from three samples in each group. Controls 1–5, healthy children; controls 6–8, patients with lower respiratory tract infection. Asthmatic children; patients 7 and 8, infants with atopic dermatitis; patient 9, child with allergic rhinitis. Controls 1–5, healthy children; controls 6–8, patients with lower respiratory tract infection.

1300) in patient 4, and 66 ± 89 (20–400) in the controls. As it has been demonstrated that most of the human mast cells originate from CD34-c-kit+ cells or from CD34-c-kit+CD13+ cells (6, 9), we investigated whether relative numbers of these particular CD34+ cell subsets were also increased in CD34+ PB cells of patients with asthma. The results are presented in Table II. There was no significant difference in the proportion of c-kit+ cells or c-kitsCD13+ cells in CD34+ cells between asthmatic children and normal controls. Comparison of maturation properties of 6-wk cultured mast cells between asthmatic patients and normal controls

Finally, we compared intracellular levels of histamine and proteases of 6-wk-old cultured cells between asthmatic subjects and normal individuals. To estimate the cellular amounts of tryptase and chymase protein, we measured protease enzymatic activity in a total of 5 × 10⁶ cells, as described by Xia et al. (20). In addition, we used the cultured mast cells derived from G-CSF-mobilized CD34+ PB cells of nonasthmatic individuals as controls, because of the paucity of mast cells grown from normal steady-state CD34+ PB cells. There were no significant differences in intracellular histamine content and tryptase/chymase enzymatic activities between the two groups. The histamine concentration of 5 × 10⁶ 6-wk-old cultured cells grown with SCF (10 ng/ml) + TPO (10 ng/ml) from CD34+ PB cells was 1508 ± 532 nM (826–2197 nM) in asthmatic patients, and 2097 ± 1079 nM (739–3667 nM) in controls. Tryptase enzymatic activity of them was 5284 ± 2124 μM (3434–9336 μM) in asthmatic patients, and 3519 ± 1439 μM (1634–5631 μM) in controls. Chymase enzymatic activity of them

Table I. An increase in mast cell colony-forming cells in CD34+ PB cells from asthmatic patients

<table>
<thead>
<tr>
<th>Number of Mast Cell Colonies</th>
<th>SCF</th>
<th>SCF + TPO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthmatic patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 1</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Patient 2</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Patient 3</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Patient 4</td>
<td>9</td>
<td>22</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>6.8 ± 1.7*</td>
<td>15.0 ± 4.8*</td>
</tr>
<tr>
<td>Normal controls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control 1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Control 2</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Control 3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Control 4</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.5 ± 1.7</td>
<td>3.0 ± 1.4</td>
</tr>
</tbody>
</table>

*CD34+ cells from PBMCs of asthmatic patients or normal controls were sorted as a single cell into the individual wells of a 96-well culture plate containing 10 ng/ml of SCF with or without 10 ng/ml of TPO. Aggregates were scored as colonies, if the constituent cells numbered 20 or more at 4 wk.

, Significantly different from normal controls (p < 0.005).

Table II. Surface marker expression on CD34+ PB cells of asthmatic patients

<table>
<thead>
<tr>
<th>CD34+ PB Cells</th>
<th>% of c-kit+ cells</th>
<th>% of c-kit+CD13+ cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthmatic Patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 1</td>
<td>61</td>
<td>14</td>
</tr>
<tr>
<td>Patient 2</td>
<td>65</td>
<td>25</td>
</tr>
<tr>
<td>Patient 3</td>
<td>66</td>
<td>16</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>64.0 ± 2.6</td>
<td>18.3 ± 5.9</td>
</tr>
<tr>
<td>Normal Controls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control 1</td>
<td>63</td>
<td>30</td>
</tr>
<tr>
<td>Control 2</td>
<td>71</td>
<td>11</td>
</tr>
<tr>
<td>Control 3</td>
<td>58</td>
<td>22</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>64.0 ± 6.6</td>
<td>21.0 ± 9.5</td>
</tr>
</tbody>
</table>

*Expression of c-kit and CD13 on CD34+ PB cells was analyzed by flow cytometry using FITC-conjugated anti-CD34 mAb, PE-conjugated anti-c-kit mAb, and PC5-conjugated anti-CD13 mAb.

FIGURE 2. Comparison of mast cell production by CD34+ PB cells under stimulation with stem cell factor + thrombopoietin between patients with allergic diseases and nonallergic controls. CD34+ PB cells (2 × 10⁴) from patients with allergic diseases and nonallergic controls were cultured in a well containing 2 ml of serum-deprived liquid culture medium supplemented with 10 ng/ml of SCF plus 10 ng/ml of TPO. After 6 wk, the viable cells were enumerated. Patients 1–6, asthmatic children; patients 7 and 8, infants with atopic dermatitis; patient 9, child with allergic rhinitis. Controls 1–5, healthy children; controls 6–8, patients with lower respiratory tract infection.

FIGURE 3. Dose response of mast cell generation by CD34+ PB cells to SCF. CD34+ PB cells (1 × 10⁴) were plated with SCF in concentrations ranging from 1 to 100 ng/ml and TPO at 10 ng/ml. At 6 wk, the numbers of progeny were counted. The results shown (mean ± SD) were derived from three samples in each group. ■, Asthmatic children; ○, normal controls. *, Significantly different from the values obtained by normal controls (p < 0.02).
was 16.0 ± 8.8 μM (7.5–28.8 μM) in asthmatic patients, and 28.5 ± 23.8 μM (3.7–62.1 μM) in controls.

Discussion

In the culture containing CD34+ cord blood cells and SCF at 10 ng/ml, a progressive, steady increase in mast cell production was achieved during 50 wk (17). When G-CSF-mobilized CD34+ PB cells were target cells, SCF alone induced the generation of significant numbers of mast cells for up to 6 wk. However, the number of cultured cells decreased at 8 wk of culture. A large portion of 4-wk progeny grown from CD34+ cord blood cells reacted with anti-tryptase mAb, but were negative for chymase (17). At 36 wk, a vast majority of the cord blood-derived cultured cells became positive for chymase. In contrast, immunoreactivity for chymase appeared markedly earlier in mast cells derived from mobilized CD34+ PB cells. A great part of the cultured cells generated from steady-state CD34+ PB cells of normal controls or from CD34+ PB cells of asthmatic patients were also positive for two types of protease at 6 wk. These lines of evidence suggest the age-related advance in mast cell maturation.

Röttem et al. (7) demonstrated that IL-3 substantially increases the numbers of mast cells grown with SCF from CD34+ PB cells. In contrast, Valen et al. (12) found IL-3-mediated down-regulation of SCF-dependent mast cell formation in long-term cultures. In this study, the addition of IL-3 to the culture containing SCF failed to augment the generation of mast cells both from G-CSF-mobilized CD34+ PB cells and from CD34+ PB cells obtained without G-CSF. In contrast, a combination of SCF and TPO exerted a prominent synergism on the production of mast cells from CD34+ PB cells obtained with or without G-CSF treatment. The time course study of the culture containing mobilized CD34+ PB cells showed that relative numbers of both tryptase+ and chymase+ cells in the cultured cells grown under stimulation with SCF+TPO increased in parallel with the values in the cells grown with SCF alone. These results suggest that TPO can expand the SCF-dependent growth of mast cells from mobilized CD34+ PB cells without influencing the differentiation into the mast cell lineage.

It is of interest that CD34+ PB cells from stable asthmatic children generated substantially greater numbers of mast cells in response to SCF alone or SCF+TPO than did steady-state CD34+ PB cells from controls. However, such an increase in the generation of mast cells from CD34+ PB cells is unlikely observed in all types of allergic disorders. Based on the results of the flow cytometric and immunocytochemical analyses, the discrepancy does not appear to result from the difference in the percentages of the particular subsets in CD34+ PB cells and from the distinct maturation stage of the progeny between asthmatic patients and normal subjects. The single-cell culture experiments clearly demonstrated that significantly greater numbers of mast cell colonies were formed by SCF alone in the cultures containing CD34+ PB cells from patients with asthma, as compared with the values obtained by normal controls. A prominent discrepancy was also noted in the SCF+TPO-responsive mast cell progenitors. Additionally, in the presence of TPO, CD34+ PB cells of asthmatic children generated apparently higher numbers of progeny under stimulation with a suboptimal concentration of SCF than did those of normal subjects. Thus, in patients with allergic asthma, greater numbers of CD34+ PB cells appear committed to the mast cell lineage. Moreover, it is suggested that mast cell progenitors have a hypersensitivity to SCF in this disorder.

Denburg and coworkers (1–5) have proposed that activation of specific hemopoietic pathways in the BM contribute to the allergic diathesis through increased production and traffic of lineage-committed inflammatory progenitors such as those of eosinophils. Moreover, significant changes are observed in the expression of hemopoietic cytokine receptors on CD34+ cells. In particular, increased expression of IL-5 receptor α on CD34+ cells favors eosinophilopoiesis, and may thus contribute to the subsequent development of blood and tissue eosinophilia. In vivo allergen-stimulated products of cytokines may account for the increases in CFU for eosinophils and/or basophils. Actually, detectable serum IL-5 concentrations are found in a proportion of patients with acute severe asthma, but not in the same patients following oral glucocorticoid therapy or in normal controls (21). Hence, there were significant falls in circulating eosinophil/basophil progenitor counts with resolution of the asthma exacerbation on beclomethasone therapy (22). In contrast, an increase in the number of mast cell progenitors in CD34+ PB cells was observed in stable asthmatic patients. Additionally, the concentrations of SCF and TPO in venous plasma were not elevated in asthmatic children compared with the values in normal subjects (the values of SCF and TPO were 1271 ± 233 pg/ml and <0.20–0.39 fmol/ml, respectively, in asthmatic children; 1047 ± 277 pg/ml and 0.26–0.74 fmol/ml, respectively, in normal controls). Therefore, it is likely that a raised level of mast cell progenitors in CD34+ PB cells from asthmatic children is mediated through a mechanism different from hemopoietic progenitors differentiating into eosinophils or basophils.

It is demonstrated that mast cell numbers are increased in bronchoalveolar lavage fluid in relatively stable asthmatic patients (23). The active recruitment of mast cell progenitors from the circulation into the tissue may contribute to ongoing airway inflammation during asymptomatic periods.

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References


