Mast Cells Cultured From the Peripheral Blood of Normal Donors and Patients With Mastocytosis Originate From a CD34+/FcεRl- Cell Population

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Mast cells may be cultured from human peripheral blood in the presence of recombinant human stem cell factor (rhSCF). The characteristics of the cells in peripheral blood that give rise to mast cells are unknown. Because mast cell precursors in human marrow are CD34+, human peripheral blood mononuclear cells from patients with mastocytosis and normal controls were sorted on the basis of CD34 expression and the positive and negative cell populations were cultured in rhSCF, recombinant human interleukin-3 (rhIL-3), or both for 6 weeks. Cell cultures were examined every 2 weeks for total and mast cell number and cell differential using Wright Giemsa and acid toluidine blue stains and antibodies to mast cell tryptase and chymase, cell-associated histamine, and expression of CD34, c-kit, FcεRl, and FcεRII using flow cytometric analysis. The ultrastructural anatomy of mast cells was examined by electron microscopy. Peripheral blood CD34+ cells cultured in rhSCF with or without rhIL-3 gave rise to cell cultures consisting of greater than 80% mast cells by 6 weeks. CD34+ cells cultured in rhIL-3 alone did not give rise to mast cells, whereas rhIL-3 plus rhSCF increased the final mast cell number eightfold when compared with cells cultured in rhSCF alone. Mast cells increased concomitantly with a decrease in large undifferentiated mononuclear cells. CD34+ cells did not give rise to mast cells. Histamine content per cell at 6 weeks was approximately 5 pg. Electron microscopy of 4-week cultures showed immature mast cells containing predominantly tryptase-positive granules that were either homogeneous or contained lattice structures, partial scroll patterns, or central dense cores and mixtures of vesicles, fine granular material, and particles. The CD34+ population at day 0 expressed Kit (65%) and FcεRII (95%), but not FcεRI, by fluorescence-activated cell sorter analysis. In addition, CD34+-derived mast cells exhibited FcεRI in addition to Kit and FcεRII, and were negative for CD34 antigen. Patients with mastocytosis showed a higher number of mast cells per CD34+ cell cultured compared with normal controls. Thus, the mast cell precursor in human peripheral blood is CD34+/FcεRI- and gives rise to mast cells in the presence of rhSCF with or without rhIL-3, and the number of mast cells arising per CD34+ cell in culture is greater when the CD34+ cells are obtained from patients with mastocytosis compared with normal subjects.

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purity of the sorted CD34+ cell population was examined by flow cytometry using mouse anti–HPCA-2 MoAb (directed against a different CD34 epitope than the primary antibody used for the cell separation: IgG1; Becton Dickinson, San Jose, CA), and ranged from 75% to 95%. Cell viability as assessed by trypan blue dye exclusion was greater than 95%.

**Cell culture.** PBMC- and BMNC-derived CD34+ and CD34− cell populations (2 × 10^6 cells/mL) were cultured in the presence of recombinant human (rh) IL-3 (30 U/mL; Genzyme Co, Boston, MA) and rhSCF (100 ng/mL; Genzyme) alone or in combination in RPMI 1640 medium containing 4 mmol/L L-glutamine, 1 mmol/L sodium pyruvate, 100 U/mL penicillin, 100 μg/mL streptomycin, 0.1 mmol/L nonessential amino acids (Bio-liquids, Inc, Rockville, MD), 5 × 10−5 mol/L 2-mercaptoethanol (Sigma, St Louis, MO), and 10% autologous serum. The use of human serum was based on initial experiments in our laboratory, which showed that PBMC cultivated in human serum gave rise to more mast cells than when PBMC were cultivated in the presence of either bovine or fetal calf serum. Cells were cultured in 24-well plates for up to 6 weeks at 37°C in a 5% CO2 humidified atmosphere. Cells were fed twice weekly by removing one-half of the culture media and replacing it with freshly prepared media together with the appropriate growth factors. Cell number was enumerated every 2 weeks using either a hemocytometer or an automated cell counter (Counter Electronics Inc, Hialeah, FL).

**Histological stains.** At 2-week intervals, aliquots of cultured cells were spun onto glass slides in a cytocentrifuge (Shandon Instruments Inc, Sewickley, PA), allowed to air dry, and stained with Wright-Giemsa using an Ames Hematek automated slide stainer (Ames). Slides were examined at high magnification (×1000), using oil immersion, to identify unstained cells on the slides.

**Immunohistochemistry.** Cytocentrifuge preparations were subjected to immunohistochemical labeling for tryptase and chymase to determine the presence and phenotype of mast cells.15,16 In brief, after Carnoy’s fixation, inhibition of endogenous peroxidase, and incubation with murine nonimmune serum, slides were incubated for 1 hour at room temp with a mixture of alcohol-phosphatase-conjugated murine antitryptase MoAb (33-AP; 6 pg/mL; Chemicon, Temecula, CA) and biotinylated murine antichymase MoAb (B7-B; 4 pg/mL, Chemicon). Tryptase-positive cells were stained blue by the addition of fast blue RR and naphthol AS-MX phosphate. Slides were then washed and chymase-positive cells were visualized in brown using indirect immunoperoxidase staining.15 Percentages of total cells comprising mast cells were determined under phase contrast microscopy to identify unstained cells on the slides.

**Electron microscopy.** CD34+ 4-week cultures were prepared for chymase and tryptase labeling and electron microscopy as described.15 Briefly, cell suspensions were fixed in a mixture of 2% paraformaldehyde and 1.5% glutaraldehyde in 0.1 mol/L sodium cacodylate buffer, pH 7.3, for 3 hours at room temperature. After washing with cacodylate buffer, the cells were suspended in warm 2% agarose and centrifuged. Cell pellets were postfixed for 1 hour at room temperature in cacodylate-buffered 1% OsO4, dehydrated in a graded ethanol series, and embedded in Embed 812/Araldite 502. Thin sections were cut and mounted on uncoated nickel grids. For immunolabeling, sections on grids were placed on a 0.56 mol/L sodium cacodylate buffer, pH 7.3, for 4 hours at room temperature. After washing with cacodylate buffer, the cells were fixed in aqueous solution of sodium metaperiodate for 70 minutes at room temp, washed with water followed by PBS, and incubated with goat IgG (0.5 mg/mL) for 1 hour at room temperature. Grids were incubated overnight at 4°C with either murine antitryptase MoAb (48 μg/mL, Chemicon) or murine antichymase polyclonal antibody (generous gift from Dr N. Schecter, Philadelphia, PA) in PBS containing 0.1% BSA. Sections were rinsed for 5 minutes each with 0.5 mol/L Tris, pH 7.2, Tris-buffered saline, and Tris containing 0.2% BSA. Sections were placed in Tris containing 1% BSA, pH 8.2, for 5 minutes followed by goat antimouse IgG bound to 10 nm gold for 1 hour at room temperature. Sections were rinsed for 5 minutes each in Tris containing 0.2% BSA, Tris-buffered saline, and water. Controls included incubation with preimmune IgG and omission of the primary antibody. Sections were stained for 15 minutes with aqueous uranyl acetate and examined in a Philips 300 electron microscope (Philips, Mahwah, NJ).

**Histamine assays.** To determine cell-associated histamine, aliquots of cells were washed, resuspended in PBS at a concentration of 5 × 10^6 cells/mL, and placed in a water bath at 100°C for 10 minutes. Samples were then analyzed for histamine content using an immunosay that uses MoAbs raised against acylated histamine.14 (Amac Inc, Westbrook, ME).

**Flow cytometry analysis.** Cell surface marker expression was assessed by flow cytometry. At designated times, cells were washed twice by centrifugation at 800g for 10 minutes and resuspended in Hanks’ Balanced Salt Solution (HBSS) without calcium, magnesium, or phenol red, containing 0.2% BSA at a concentration of 10^7 cells/mL. Analyses were then made by direct immunofluorescence for Kit expression using a phycoerythrin (PE)-conjugated mouse MoAb directed against Kit (IgM; Amac), for CD34 expression using fluorescein isothiocyanate (FITC)-conjugated mouse anti-CD34 (HPCA-2; Becton Dickinson), and for FcRII using FITC-conjugated human IgE as described.17,18 and by indirect immunofluorescence for FcγII using biotin-conjugated 2.4G2 MoAb and streptavidin PE. Nonspecific fluorescence was assessed by substituting isotype-specific antibody for the MoAb in the case of Kit, CD34, and FcγII, and by preincubating an aliquot of the cells with 100 μg/mL of purified monoclonal IgE before adding the FITC-conjugated IgE in the case of FcγRII. Flow cytometric analysis was performed on an Epics 753 (Coulter Electronics) with an Argon laser (Coherent Inc, Palo Alto, CA) tuned to 488 nm, wavelength 300 mW. Multiparameter data acquisition and display system software (Coulter Electronics) and a four-decade logarithmic amplifier were used for statistical analysis and the data displays.

**RESULTS**

**Kinetics of the appearance of mast cells from PBMC-derived CD34+ cells.** We have previously shown that human mast cells originate from CD34+ cells within the BM.13 Because mast cell precursors appear to be present in PB,8 we hypothesized that mast cell progenitors in blood were also CD34+. PBMC were sorted on the basis of CD34 expression, and the positive and negative populations were cultured in the presence of either rhIL-3, rhSCF, or both. Approximately 5 × 10^5 CD34+ cells were isolated per 10^7 total PB nucleated cells. When CD34+ were cultured in the presence of rhIL-3 alone, total cell number decreased over time, and no mast cells could be identified (Fig 1A). Cells cultured in the presence of rhSCF or rhSCF and rhIL-3 increased in average total cell number from 1 × 10^6 cells on day 0 to 1.1 × 10^6 and 8.4 × 10^6 cells at 6 weeks, respectively (Fig 1B and C). Mast cell number in these cultures similarly increased from 0 on day 0 to an average of 0.8 × 10^6 and 8 × 10^6 at 6 weeks, respectively. Thus, approximately 1 mast cell was obtained per CD34+ cell cultured in rhSCF alone, and 8 mast cells were obtained per CD34+ cell cultured in rhSCF plus rhIL-3. CD34+ cells decreased in number under all conditions and did not give rise to mast cells (Fig 1A, B, and C). Unsorted PBMC cultured in rhSCF with or without rhIL-3 gave rise to similar numbers of mast
cells from a starting population of $10^6$ nucleated cells (data not shown). These experiments show that mast cell progenitors in the peripheral circulation are CD34+, and that there are no CD34- mononuclear cells in the peripheral circulation that can give rise to mast cells. SCF is thus both necessary and sufficient for the growth of mast cells from human PB, although IL-3 enhances SCF-dependent mast cell growth. We have observed similar responses to SCF and IL-3 using murine PBMC-derived mast cells.19

To further explore the fate of CD34+ cells cultured in the presence of rhSCF or rhSCF and rIL-3 (Fig 1B and C), we next examined the type of cells observed in these cultures. At day 0, cultures were composed of 93% large mononuclear cells, 6% myelocytic cells, and 1% monocytes (Fig 2A and B). No metachromatic cells, as assessed by acid toluidine blue staining, were noted. With time, the percentage of large mononuclear cells decreased, concomitant with an increase in the percentage of metachromatic cells. The percentage of monocytes under both conditions increased slightly at 4 weeks to an average of 6% of total cells in culture, whereas the number of myelocytes decreased. By 6 weeks, more than 80% of cells cultured in rhSCF alone were metachromatic, whereas more than 90% of cells cultured in rhSCF and rIIl-3 exhibited metachromatic staining. In data not shown, by 8 weeks virtually all cells were metachromatic under both conditions. Similarly, at 2 weeks, about 50% of metachromatic cells exhibited morphologic characteristics of basophils, whereas at 4 weeks 85% were recognized as mast cells. Cell counts by 6 weeks were confirmed by immunohistochemistry for tryptase (see below).

**Characterization of cultured cells.** By 6 weeks, PBMC-derived CD34+ cells, as shown under phase microscopy in Fig 3A, primarily consisted of mast cells as determined by acid toluidine blue staining (Fig 3B). Cells were also examined for the expression of mast cell tryptase and were uniformly positive for this enzyme found in both mucosal and connective tissue type mast cells (Fig 3C). Occasional cells

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**Fig 1.** Kinetics of the appearance of mast cells from PBMC-derived CD34+ and CD34- cells. Cells were cultured for 6 weeks in the presence of either rhIL-3 (A), rhSCF (B), or both (C). Total CD34+ (circles) and CD34- (squares) cell number (open symbols) and mast cell number (solid symbols) were enumerated every 2 weeks. Cells were identified as mast cells using acid toluidine blue staining. PB was obtained from 8 different patients with indolent mastocytosis. In each case, data for (A), (B), and (C) was obtained in parallel for each individual donor. Data are presented as mean ± SEM (n = 9, 1 patient was studied twice).

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**Fig 2.** Cell types developing in PBMC-derived CD34+ cell cultures (see Fig 1B and C) grown in the presence of rhSCF (A) or rhSCF and rIIl-3 (B). Cells were identified on Wright-Giemsa-stained cytospin preparations as either large mononuclear cells (□), myelocytes (▲), monocytes/macrophages (△), basophils (●), or mast cells (Θ). Cells were obtained from PB of patients with indolent mastocytosis (see Fig 1 legend). Data are presented as mean ± SEM (n = 9).
Fig 3. Mast cells cultured from PBMC-derived CD34\(^+\) cells. Cells shown were cultured in the presence of rhIL-3 and rhSCF for 6 weeks, and examined under phase microscopy (A, original magnification \(\times 400\)), or after staining with acid toluidine blue (B, original magnification \(\times 1,250\) under oil) or using antibody to tryptase (C, original magnification \(\times 1,250\) under oil).

were lightly positive for chymase (data not shown), an enzyme associated with connective tissue mast cells. Cultures were also examined by electron microscopy at 4 weeks, when the majority of cells in culture were identified by light microscopy as mast cells. As can be seen in Fig 4, ultrastructural examination of PBMC-derived CD34\(^+\) cells showed immature mast cells (Fig 4A). These cells exhibited a wide variety of characteristic features of human mast cells cultured from other tissues.\(^{20}\) These characteristics included mature granules with homogeneous dense material (Fig 4B), granules containing characteristic lattice or crystalline arrays (Fig 4C), and granules with partial or nondiscrete scroll patterns (Fig 4D). Immature granules contained central dense cores and mixtures of vesicles, fine granular material and particles (Fig 4E). Immunogold labeling for tryptase was positive in all granule types (Fig 4A through D). A minority of granules were also faintly positive for chymase (data not shown). The cell nuclei were large and often lobulated. The surface showed numerous short narrow cytoplasmic extensions. Cytoplasmic organelles included clusters of lipid bodies, mitochondria, golgi, and free ribosomes, all consistent with immature mast cells.

To further characterize the cells developing in the presence of rhSCF and rhIL-3 in culture, we next examined cell associated histamine. As can be seen in Fig 5, histamine content per cell increased from an average of 0.01 ± 0.01 pg/cell at week 1 to an average of 5.00 ± 0.45 pg/cell at 4 weeks, after which the histamine per cell did not significantly change. This histamine content per cell at 6 weeks is similar to the amount of histamine reported to be present in human lung-derived mast cells.\(^{21}\)

**Surface marker expression of PBMC-derived CD34\(^+\) cells.** Murine studies on the differentiation of mast cells have suggested that mast cell progenitors express Fc,RI and Fc,RII.\(^{22}\) Thus, we examined the CD34\(^+\) cell population initially and after 6 weeks in culture for the expression of these cell surface molecules as well as for Kit and CD34. At day 0, the majority of cells expressed CD34 (85%), Kit (50%), and Fc,RII (85%), but no Fc,RI (Fig 6A through D). CD34\(^+\) cells incubated with human IgE\(\text{a}\), followed by incubation with goat antihuman IgE 10 nm gold did not show surface-associated human IgE, consistent with the absence of significant numbers of Fc,RI (data not shown). Within the CD34\(^+\) cells, 65% were Kit\(^+\) and 95% were Fc,RII\(^+\). At 6 weeks, cells now expressed Fc,RI, Fc,RII, and Kit, but no CD34 (Fig 6E through H). CD34 expression was found to be lost within 3 days in culture and before Fc,RI could be detected (data not shown). Thus, circulating CD34\(^+\) mast cell progenitors do not express significant membrane-associated Fc,RI.

**Kinetics of the appearance of mast cells from BMMC-derived CD34\(^+\) cells.** We have previously shown that mast cells arise from CD34\(^+\) cells harvested and sorted from the BM by immunomagnetic beads.\(^{2}\) To compare the kinetics of the appearance of mast cells from BMMC-derived CD34\(^+\) cells and from PBMC-derived CD34\(^+\) cells, we next examined the kinetics of appearance of mast cells from BMMC-derived CD34\(^+\) cells in the presence of rhSCF and rhIL-3. The number of CD34\(^+\) cells generated from BMMC was on the average approximately 13 times higher than from PBMC (6.8% compared with 0.5%, respectively). As can be seen in Fig 7, only CD34\(^+\) cell gave rise to mast cells. The temporary peak of total cell number at the second week suggests that BMMC-derived CD34\(^+\) cells may initially proliferate and give rise to more committed progenitor cells of lineages other than the mast cell lineage, but that eventually only the mast cell progenitors survive under the conditions chosen. Differential counts at the second week showed that 95% of cells were large mononuclear cells (data not shown). At 6 weeks, the average total cell number and mast cell number were similar to the number of cells that were cultured from PBMC-derived CD34\(^+\) cells.
Kinetics of the appearance of mast cells from PBMC-derived CD34+ cells from patients with mastocytosis compared with normal controls. We next examined the kinetics of the appearance of mast cells in culture to determine if mast cell number was influenced by whether or not the CD34+ cell population was obtained from patients with mastocytosis or normal donors. For this comparison, the kinetics of appearance of mast cells arising from CD34+ cells obtained from patients with indolent systemic mastocytosis and in the presence of rhIL-3 and rhSCF as shown in Fig 1C is repeated in Fig 8 and compared with the appearance of mast cells from CD34+ cells obtained from 3 normal subjects and 2 patients with aggressive mastocytosis. As can be seen in Fig 8, the number of mast cells observed at 4 weeks was similar when the CD34+ cells were obtained from patients with indolent systemic mastocytosis or normal subjects, although by 6 weeks an approximate twofold increase in mast cells was seen in cultures from indolent systemic mastocytosis patients compared with cultures obtained from normal subjects. In contrast, when CD34+ cells were obtained from patients with aggressive mastocytosis, both total cell number and mast cell number was increased at 2, 4, and 6 weeks when compared with data obtained from patients with indolent systemic mastocytosis and from normal subjects. The basis for the disparity in the growth curves is under exploration. Preliminary experiments suggest that these results are not influenced by serum of specific donors. In one instance, CD34+ cells from a normal subject exhibited identical growth pattern characteristics when grown in autologous normal serum or heterologous serum from a patient with aggressive mastocytosis. In a second experiment, CD34+ cells from a patient with aggressive mastocytosis were cultured for 3 weeks in autologous serum, rhIL-3, and rhSCF. The cells were then divided, with half of the cells cultured in autologous serum, rhIL-3, and rhSCF, and the second half cultured in heterologous normal human serum, rhIL-3, and rhSCF. After 3 weeks, the total mast cell number was similar in both cultures.

DISCUSSION

The data presented here clearly show that the mast cell precursor in human PB is CD34+ (Fig 1). These circulating CD34+ cells morphologically resemble large mononuclear cells and contain no granules (Fig 2). They bear no measur-
Histamine content of PBMC-derived CD34+ cells cultured for 6 weeks in the presence of rhIL-3 and rhSCF. Histamine content was determined weekly using a radioimmunoassay (see Materials and Methods). Cells were obtained from 3 patients with indolent mastocytosis. Data are presented as mean ± SEM (n = 3).

The CD34+ cells by 6 weeks in culture consisted of greater than 80% mast cells. These mast cells were toluidine blue+, expressed Fc,RI, contained histamine, and stained with antibody to mast cell tryptase (Fig 3). Less than 3% of cultured mast cells at 6 weeks stained with antibody to chymase. Tryptase+/chymase- mast cells are generally considered to be of the mucosal phenotype, and it may be that additional cytokines are required for the expression of chymase, which is a marker of the connective tissue mast cell phenotype. Modulation of the mast cell granule phenotype has been described for murine mast cells.3

The ultrastructural anatomy of mast cells has been described for mast cells from human tissues, and mast cells either arising from cord blood or fetal liver.14 However, in previous reports in which mast cells were grown from adult human blood, no ultrastructure was reported.6 For this reason, we performed a detailed analysis using electron microscopy of mast cells arising in our cultures. Ultrastructural granule patterns in mast cells cultured from adult blood in this report were similar to those reported for mast cells from cord blood or fetal liver,7,14 in that they variably contained granules with homogeneously dense contents, vesicles, non-discrete scrolls, and particles. However, mast cells from adult blood differed in that granules containing lattice or crystaline arrays could also be identified (Fig 4C). The crystal-containing granules are usually considered to be characteristic for connective tissue type mast cells, but have been seen when immature human cord blood-derived mast cells were cocultured with 3T3 fibroblasts.20

rhSCF is required for the development of mast cells from the CD34+ cell population in marrow and blood. This is not surprising, because it has been reported that mast cells can be cultured from human cord blood, adult PB, and fetal liver cells in rhSCF alone.7,10 However, it was unexpected that rhIL-3 would increase mast cell yield eightfold. The use of rhIL-3 and human sera (in place of fetal calf serum) in the presence of rhSCF, as first reported here, provides for a culture system that reproducibly gives rise to substantial numbers of human mast cells.

As shown in Figs 2 and 7, CD34+ cells from human PB or BM cultured in rhSCF with or without rhIL-3 give rise to a cell population dominated by mast cells at 6 weeks. Both rhIL-3 and rhSCF are growth factors that effect multiple hematopoietic cells early in differentiation. However, in the case of hematopoietically derived cells such as neutrophils or eosinophils, receptors for SCF appear to be downregulated in number and terminal differentiation requires specific growth factors such as granulocyte colony-stimulating factor or IL-5. In contrast, mast cells continue to express c-kit (Fig 6), and thus continue to develop in these cultures to the point at which by 6 weeks few if any other cell types can be identified.

This flow cytometric analysis of PBMC-derived CD34+ cells. Cells were cultured for 6 weeks in the presence of rhIL-3 and rhSCF, and analyzed at day 0 (A through D) and at 6 weeks (E through H) for the expression of CD34 (A and E), c-kit (B and F), Fc,RI (C and G), and Fc,RII (D and H). (---) The specific antibody; (---) the control antibody. Data presented represent results of experiments performed on blood obtained from patients with indolent mastocytosis. Similar results were obtained on cells of normal subjects.
An unexpected observation in this report was that CD34+ cells from patients with aggressive mastocytosis yield increased mast cell numbers by 6 weeks when compared with CD34+ cells obtained from patients with indolent mastocytosis or normal subjects (Fig 8). Preliminary experiments suggest that this is not caused by a serum factor as suggested by data that some forms of mastocytosis are associated with increased amounts of immunoreactive SCF in the dermis, but rather by an inherent property of the CD34+ cell population itself, perhaps reflecting a c-kit mutation. What is intriguing about this observation is that it also parallels the in vivo data, which show that patients with aggressive mastocytosis more rapidly accumulate mast cells than those with indolent mastocytosis. The differences between mast cell numbers obtained from CD34+ cell populations from patients with indolent mastocytosis is less remarkable when compared with normal subjects.

We have recently observed that mouse PBMC cultured in recombinant mouse (rm) SCF alone give rise to a virtually pure population of mast cells by 2 weeks, and mast cell number increased by the addition of rmIL-3. Given the knowledge that human cells in culture characteristically grow more slowly that mouse cells in culture, the data obtained from the human studies reported here are virtually identical to similar studies in the mouse. This is the first demonstration then that mouse and human mast cell precursors in marrow (Fig 7) and PB (Fig 1) respond in a virtually identical fashion to mast cell growth factors given the improved culture conditions for mast cell cultures reported here. Compared with a previous study of PBMC cultured in rhSCF that by 35 days yielded a population of 0.2 to 7% mast cells, we obtained a higher purity of mast cells and in greater number that we attribute to the use of autologous human serum. This appears to resolve the long-standing dispute as to apparent differences in mast cell growth characteristics between mice and humans, and supports again the use of mouse models to study the growth and differentiation of immunologic effector cells. Additionally, the improved culture conditions for human mast cells reported here should permit the wider study of human mast cell biology.

Hematopoietically derived cells, including neutrophils, eosinophils, basophils, and monocytes, circulate in mature form in blood. This study shows that mast cells clearly differ from this behavior. Not only do they not circulate in mature form, but they do not appear as sparsely granulated Fc,RI+ mast cell precursors, as has been suggested.22 Rather, human mast cells in PB are derived from a CD34+, Fc,RI+ cell population. Not only is this true in normal subjects, but also for patients with mastocytosis, arguing against clonal expansion of differential mast cells in the etiology of this disease.

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Mast cells cultured from the peripheral blood of normal donors and patients with mastocytosis originate from a CD34+/Fc epsilon RI- cell population

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