Pro-Con Symposium:
Are Basophils Important in Allergy?

Pros

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Outline

- Differences between human basophils and mast cells (they act complementary).
- Only basophils can produce IL-4, which induces Th2 cells from naïve T cells, in the primary immune response.
- Human basophils but not mast cells can release cysteinyl leukotrienes and histamine in the late phase asthmatic response.
- Murine basophils have a variety of unique roles in immunity and inflammation.

Basophils and Mast Cells

They resemble each other in morphological and functional features.
Mast cells have euchromatin (=capable of proliferating), while basophils have heterochromatin (=end stage cells).

Dvorak AM, Sciuto TE. Int Arch Allergy Immunol. 2004

We have been investigating the gene expression profiles of various cell types related to allergic diseases.


Basophils dominantly express IL-4, IL-13, IL-3R, CCR2 and CCR3 among all cytokine-chemokines and their receptors compared to other cells.

Mast cells dominantly express CCL2 and CCL7 among all chemokines compared to other cells. Also, they express IL-4R, IL-3 and PGD2 enzymes at high levels (data not shown).

Mast cells and basophils act complementary. Activated mast cells tend to express cytokines and chemokines whose receptors basophils highly express. Basophils also tend to express cytokines whose mast cells express high levels of receptors.

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IL-4 but not IL-13 is indispensable to induce Th2 cells from naive T cells, although IgE production by B cells can be supported by IL-4 or IL-13.
Basophils but not (human) mast cells produce IL-4 and thereby induce IgE production by B cells.

Even natural helper cells or innate lymphoid cells capable of producing IL-5 and IL-13 at high levels do not produce IL-4.

Basophils are capable of producing IL-4 even in the absence of IgE.

Allergen Der p1 can induce production of IL-4 by basophils without IgE.
Basophil-derived IL-4 may be indispensable to induce Th2 cells from naïve T cells.

Allergen uptake

Induction of Th2 cells

Production of IgE antibody

Allergic reactions

Mast cell activation

Reentry of the allergen

IL-4

IL-13

Allergen presentation to naïve T cells

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Basophils produce LTC₄ at 30-fold higher levels compared to eosinophils.

<table>
<thead>
<tr>
<th>Secretagogues:</th>
<th>Basophils</th>
<th>Eosinophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>C5a, C3a, fMLP</td>
<td>PA (weak)</td>
<td>C5a, C3a, PAF fMLP (weak)</td>
</tr>
<tr>
<td>MBP, polyamines</td>
<td>Cys-LTs release from eosinophils and basophils</td>
<td>Tryptase (weak)</td>
</tr>
<tr>
<td>MCP-1, SDF-1α, MIP-1α antigen</td>
<td>None</td>
<td>None</td>
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<table>
<thead>
<tr>
<th>Mediators:</th>
<th>Basophils</th>
<th>Eosinophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histamine, 1 μg/10⁶</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>LTC₄, 50 pmol/10⁶</td>
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<td>None</td>
</tr>
<tr>
<td>IL-4, 1000 pg/10⁶</td>
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<td>None</td>
</tr>
<tr>
<td>IL-13, 200 pg/10⁶</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Tryptase (weak)</td>
<td>None</td>
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Basophils are the majority among the leukocytes accumulated into the lungs of the fatal asthmatics.


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Basophils play an important role in late phase asthmatic response by releasing cysteinyl leukotrienes.


a. Basophils drive Th2 cell differentiation during the primary immune response. In the draining lymph nodes, basophils secrete IL-4, which induce the differentiation of naive T cells into Th2 cells in cooperation with antigen-presenting dendritic cells.

b. Basophils enhance antibody production in the secondary immune response. In antigen-sensitized animals, following re-exposure to the same antigen, basophils efficiently bind free antigens through IgE–FcεRI complexes, become activated and secrete IL-4 and IL-6. These antigen-stimulated basophils interact with antigen-specific B cells and Th cells.

Basophils are important in allergy. Because:

- Basophils and mast cells act complementary, that is, basophils have unique roles in allergy.
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