Donor Sensitivity to Basophil Activation by Eosinophil Granule Major Basic Protein

L.M.		Zheutlin
S.J.		Ackerman
G.J.		Gleich
L.L.		Thomas

Department of Immunology/Microbiology, Rush Medical College, Chicago, Ill.;
Departments of Immunology and Medicine, Mayo Clinic and Foundation and Mayo
Medical School, Rochester, Minn., USA

Abstract

Leukocytes of 22 individuals were incubated with a suboptimal concentration of eosinophil granule major basic protein and the amount of histamine release was determined. Cells from 20 of the 22 donors had a histamine release of $\geq 15\%$. The use of selected donors on repeated occasions revealed significant variability in individual donor responsiveness. The findings support a role for major basic protein activation of human basophils in allergic reactions.

Correspondence to: Dr. Larry L. Thomas, Department of Immunology/Microbiology, Rush Medical College, 1753 West Congress Parkway, Chicago, IL 60612 (USA)

The presence in eosinophils of enzymes that degrade basophil and mast cell mediators led to the hypothesis that eosinophils dampen allergic reactions [1]. Recent evidence suggests, however, that eosinophils may actually contribute to the pathogenesis. Major basic protein (MBP), a 9,300-dalton basic poly-peptide localized in the crystalloid core of the eosinophil granule [2], is toxic for mammalian cells including respiratory epithelium [3], is present in elevated concentrations in fluids of patients with eosinophilia [2, 3], and is deposited at sites of bronchial epithelial damage [4] and in urticarial lesions [5]. A pathogenic role for eosinophils and MBP was strengthened by the finding that MBP also stimulated noncytolytic histamine release from human basophils and rat mast cells [6]. To assess differences in individual donor sensitivity to basophil activation by MBP, we measured the amount of histamine release stimulated by a single concentration of MBP from cells of 22 individuals.

Leukocytes isolated by dextran sedimentation or basophil-containing mononuclear cells isolated by Ficoll-Hypaque density centrifugation were incubated with 3.4×10^{-6} M purified human MBP for 45 min at 37 °C. The resultant histamine release values for the 22 donors ranged from 4–54% (fig. 1, left panel). Basophils from the majority of the individuals tested released 15–30% of their histamine content, while basophils from a smaller percentage of donors released $\geq 40\%$ of their histamine content. Cells of two individuals yielded $< 5\%$ histamine release. To assess the reproducibility of the response of individual donors, cells of 5 individuals were tested on repeated occasions with the same concentration of MBP (fig. 1, right panel). Cells of 3 donors (■, O, A) yielded fairly consistent histamine release values but cells of 2 of the 5 donors (·, Δ) exhibited considerable variability. The basis of this variability is being investigated. An additional finding of this study is that, thus far, atopic individuals cannot be distinguished

from nonatopic individuals in their response to MBP. 10 of the 22 individuals tested were atopic, including 3 of the individuals (■, O, A) depicted in the right panel of figure 1.

These results demonstrate that basophils of individual donors exhibit different degrees of sensitivity to MBP. Although cells of a few individuals were comparatively unresponsive, cells from the majority of donors yielded significant histamine release ($> 15\%$), with some exhibiting marked sensitivity ($> 40\%$ histamine release). The finding that a concentration of MBP detected clinically [3] stimulated significant histamine release from the basophils of a majority of the individuals tested reinforces the potential of MBP activation of human basophils as a pathogenic mechanism in allergic reactions and other disorders characterized by eosinophilia.

MPB-Stimulated Histamine Release

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Fig. 1. Stimulation of histamine release by 3.4×10^{-6} M MBP. The histamine release values obtained for 22 individuals are depicted by the symbols in the left panel. In the right panel, histamine release values obtained for 5 individuals (■, O, •, Δ, ▲) in repeated experiments are presented.