Molds Modulate the Release of Histamine and Sulfidoleukotrienes from Human Basophils

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Introduction

Mediator release from human basophils or mast cells can be initiated by a range of immunological, chemical and physical stimuli [1,2]. In addition, bacteria or viral organisms are able to modulate spontaneous and allergen-induced mediator release from basophils in the absence of microbe-specific IgE [3]. Previous studies have shown an enhancing capacity of mold preparations upon spontaneous and allergen-induced basophil histamine release (HR) in the absence of mold-specific IgE in atopic donors, whereas basophils of nonatopic individuals remained mostly unaffected [4]. We have now assessed the effects of mold preparations upon HR and production of sulfidoleukotrienes (sLTs) from peripheral blood leukocytes (PBLs) in response to a range of stimuli.

Materials and Methods

Colonies of *Aspergillus niger*, *Aspergillus fumigatus*, *Alternaria tenuis* and *Cladosporium herbarum* were grown on Sabouraud agar and kindly provided by Dr. P. Seidl (Institut für Mikrobiologie, Technische Universität, Munich). Molds were harvested, mechanically homogenized and filtered (0.45 µm pore size). Preparations of *A. niger* and a mixture of *A. fumigatus*, *A. tenuis* and *C. herbarum* were used for stimulation at a final protein concentration of 7 µg/ml. Suspensions of PBLs containing basophils were obtained by dextran sedimentation outside the pollen season from the peripheral blood of 10 individuals with seasonal rhinoconjunctivitis who had no specific serum IgE to the molds used. Cells (2×10⁷/ml; duplicate tubes) were incubated for 30 min with nontoxic aliquots (Trypan blue exclusion) of mold preparations and subsequently stimulated with anti-IgE (10⁻²), relevant allergen (3 birch, 5 grass, 1 hazel, 1 alder; intracutaneous test solution, 10⁻²) or Ca ionophore (10⁻⁷mol/l). Released histamine in the supernatants was measured spectrofluorometrically and expressed as percentage of total histamine content after correction for spontaneous HR. Sulfidoleukotrienes in

the supernatants were determined by EL-ISA. The Mann-Whitney U test was used for statistical evaluation.

Results and Discussion

Results are shown in figures 1 and 2. Preincubation with mold preparations, particularly *A. niger*, enhanced HR and sLT production in response to the secretagogues to a varying degree, depending on the activating signal and the origin of the individual cell sample. Thus, in the absence of mold-specific IgE, mold components can enhance basophil reactivity and this could be relevant for clinical disease.

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Fig. 1. Influence of mold components upon spontaneous and secretagogue-induced HR from cell suspensions containing basophils of 10 individuals with seasonal rhinoconjunctivitis. Stimulation was performed with aeroallergens, anti-IgE or Ca ionophore alone (O) or after preincubation with an *A. niger* (•) or a mixed-mold (*) preparation. Medians and significant differences (## < 0.01) are indicated.

There is also evidence of potentiation of HR from basophils in the presence of certain bacteria and viruses [3, 5]. Bacteria-dependent modulatory effects are thought to be mediated at least in part through interaction between bacterial wall carbohydrates or glycoproteins and lectin-like binding sites on mast cells or basophils [6]. In the case of viruses, envelope glycoproteins may exert a similar role. Whether the mold-dependent modulatory effects are due to soluble factors or structural mold components is the subject of current experiments. Identification of the causal components will assist in evaluating the mechanisms of action.

Fig. 2. Influence of mold components upon spontaneous and secretagogue-induced sLT production from cell suspensions containing basophils of 10 individuals with seasonal rhinoconjunctivitis. For stimulation, aeroallergens or anti-IgE (a) or Ca ionophore (b) were used either alone (O) or after preincubation with an *A. niger* (•) or mixed-mold (*) preparation. Medians and significant differences (#p < 0.05; ##p < 0.01) are indicated.

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