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INNATE AND ADAPTIVE IMMUNITY CYTOKINES IN NASAL MUCOSA AND BLOOD SERUM OF ALLERGIC RHINITIS PATIENTS

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The study was aimed to evaluate the cytokine profile in nasal secretion and blood serum in patients with seasonal and perennial allergic rhinitis (AR) with a potential for additional sensitization with microbial allergens.

The inclusion criteria for AR were as follows: a diagnosis of AR for more than 2 years, the absence of nonallergic disorders of the nasopharynx, age of patients from 4 years to 60 years. Control group: healthy volunteers at the age of 3–43 years without any allergic disorders at examination. In order to evaluate the innate and adaptive immunity, the cytokine profile of blood serum (IL-4, IL-10, and TGF-β) and nasal secretion (TSLP, IL-1β, TNFα, and GM-CSF) was determined. To determine TSLP, TGF-β, IL-10, and GM-CSF concentrations, enzyme-linked immunosorbent assay kits were used (eBioscience, Bender MedSystems, R&D Systems, MN, USA).

The epithelial cells of the upper airways are capable of synthesizing TSLP where this cytokine affects DCs causing their maturation and activation. We have noticed a significant correlation (r = 0 46, p = 0 014) between the TSLP concentration in nasal secretion and allergen-specific antibodies (IgE) level to *S. aureus* enterotoxin (allergen component m80) in patients with PAR. There was a significant correlation (r = 0 56, p = 0 008) between TSLP and GM-CSF cytokine concentrations in nasal secretion of these patients. There was a significant correlation between TSLP cytokine concentrations in nasal secretion and those in allergen-specific antibodies (IgE) to the allergen component m3 of Aspergillus fumigatus in the patients with SAR (r = 0 43, p = 0 023). GM-CSF cytokine is produced by upper airway epithelial cells in an allergic inflammation. There was a significant correlation (r = 0 58, p = 0 007) between GM-CSF concentrations in nasal secretion and those in allergen-specific IgE antibodies to the allergen component d1 of *D. pteronyssinus* in patients with PAR.

Staphylococcal superantigens might be one of the stimuli of local TSLP hyperproduction by the epithelium. There was a significant correlation between GM-CSF concentrations in nasal secretion and the intensity of sensitization to a staphylococcal enterotoxin (SEB) in the patients with perennial allergic rhinitis. The patients with perennial allergic rhinitis and additional high sensitization to SEs demonstrated a higher TNFα production profile due to macrophage and T cell activation by these toxins.

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ANALYSIS OF TOXIN-NEUTRALIZING ACTIVITY OF MOUSE MONOCLONAL ANTIBODIES AGAINST PROTECTIVE ANTIGEN OF *BACILLUS ANTHRACIS*

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Anthrax exotoxin is the main virulence factor of *B. anthracis*. It consists of 3 proteins: protective antigen (PA), edema factor (EF) and lethal factor (LF). Acting in binary combinations, heptamers of PA with LF or EF forming the lethal or edema toxins (LT or ET), correspondently. Highly specific monoclonal antibodies (mAbs) can block or inhibit the action of the toxin and might be used as therapeutical agents against the threat of anthrax infection.

The aim of the study was to determine the ability of mouse mAbs against 3 (1D6F10, 4F5C7, 4F6F8, 7E5B7, 9D5G9) and 4 domain (1E10A1) PA of *B. anthracis* to neutralize the destructive influence of LT on mouse macrophage cell line J774A.1.

The toxin-neutralizing activity of mAbs was assessed by MTT assay. Four different concentrations of rPA and rLF were chosen to show the partial and complete lethal effects of this complex — from LD_{50} (0.5 μg/ml rPA and 0.1 μg/ml rLF) to LD_{100} (4 μg/ml rPA and 0.8 μg/ml rLF). Two different concentrations of mAbs were chosen to show ability to resist toxic action of LT — 4 and 40 μg/ml, that demonstrate the amount of antibodies, which can presumably bind a half of the PA molecules and its 5 times bigger quantity. As controls were used cells without treatment, dead cells and cells with the same concentrations of LT.

The strongest toxin-neutralizing effect was demonstrated by 3 mAbs of 6, which even at a low concentration in LD_{100} of LT contributed to the survival of cells above 50% (4F5C7 — 63%, 4F6F8 — 56%, 1E10A1 — 80%). In addition, excess concentration of mAb 1E10A1 completely prevented toxic damage on cells. The rest showed low activity (7E5B7 and 9D5G9) or presented a potentiating influence against LT (1D6F10).

MAb 1E10A1 can be recommended for further *in vivo* studies in animal models to confirm toxin-neutralizing activity.

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