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INTERACTION OF INTERFERON WITH OTHER IMMUNOMODULATORS REGULATING HUMAN NATURAL KILLER CELL ACTIVITY

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In our research into regulation of activity of natural killer cells (NKC), which constitute the main cell population in the natural cytotoxicity (NCT) system, we found a definite similarity in the properties of T-activin (TA), a stimulator of antibody producers and interferon (IFN), manifested in particular as stimulation of NKC activity in the presence of low effector to target (B:T) ratios was discovered [7]. Considering that the question of the origin of NKC has not yet been answered (compare [1] and [2]) this result has been regarded as evidence that all three factors are involved at a certain stage in regulation of maturation of NKC precursors. The key place of IFN in activation of NKC and induction of their maturation [14, 15] suggested that the study of regulation of NKC by IFN in combination with peptides controlling individual stages of immunity, and possessing a definite action on NKC, would lead to an understanding of the principles governing differentiation of these cells in man.

The aim of the investigation was to assess the action of reaferon (RF) (human recombinant IFN-α_2) in conjunction with regulatory peptides of varied origin on NKC activity in vitro in healthy individuals and patients with multiple sclerosis (MS). MS was chosen as the model because in this disease there is an IFN-dependent NKC deficiency [5], IFN preparations are widely used in the treatment of MS [12, 13], and definite positive results have been obtained in the clinic for nervous diseases of the N. I. Pirogov Second Moscow Medical Institute by treatment of patients with MS by T-activin, myelopide (MP), and dalargin (DL). Altogether 20 healthy blood donors (four men and 16 women) aged from 18 to 46 years and 34 patients with MS (12 men and 22 women) aged from 16 to 55 years, with a remittent course of the disease, the duration of which varied from 6 months to 12 years, and with different degrees of disability on the Kurtske scale, were investigated.

EXPERIMENTAL METHOD

Mononuclear cells (MNC) were isolated from peripheral venous blood of the healthy subjects and patients in a one-step Ficoll—Paque density gradient (Pharmacia Fine Chemicals, Sweden), d = 1.077 g/cm^3 [9].

The cytotoxic activity of NKC was determined by a radiometric method, against target cells (TC) of human erythromyeloleukemia K-562 [10], labeled with ^{3}H-uridine in a dose of 3 μCi/ml, in the modification in [3]. Combined incubation of MNC and TC was carried out for 14 h at 37°C in a humid atmosphere containing 5% CO_2. Complete nutrient medium based on RPMI-1640, used for incubation, had the following composition. RPMI-1640 (Amimed, Switzerland) 88 ml; bovine embryonic serum (N. F. Gamaleya Research Institute of Bpidemiology and Microbiology, Academy of Medical Sciences of the USSR) 12 ml, HEPES (Serva, Germany) 10 mM, glutamine 2 mM, gentamicin (Pharmachim, Bulgaria) 40 μg/ml. The E:T ratio ranged from 100:1 to 6:1.

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