SENSITIVITY OF HUMAN LYMPHOCYTES TO ANTIPROLIFERATIVE ACTION OF GLUCOCORTICOIDS AND RECEPTOR EFFICIENCY

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The immunodepressive action of glucocorticoid hormones (GCH) is largely determined by their ability to inhibit proliferation of human lymphoid cells. Marked individual differences exist in the sensitivity of lymphoid cells of different individuals to the antiproliferative activity of GCH [5, 6]. Meanwhile we know that individual differences in sensitivity to the therapeutic action of high doses of GCH in immunoinflammatory diseases are due to genetically determined differences in the number of GCH receptors (GCHR) [4]. It accordingly seems likely that individual differences in the sensitivity of lymphoid cells may be connected with genetically determined variability of GCH reception by cells.

The writers previously suggested a method of assessing the sensitivity of human lymphocytes to the antiproliferative action of glucocorticoids [2], based on the positive correlation discovered by the writers between the intensity of the proliferative response to PHA and the degree of depression of this response by dexamethasone. Using the method of regression analysis, all the blood donors investigated were divided into three groups: sensitive, intermediate, and resistant.

The aim of this investigation was to assess correlation between the type of sensitivity of a donor's lymphocytes to the antiproliferative action of dexamethasone and the characteristics of these cells with respect to GCH reception.

EXPERIMENTAL METHOD

Nine healthy blood donors were tested. Methods of setting up the blast transformation reaction and of determining the type of sensitivity of the lymphocytes to the antiproliferative action of dexamethasone were described previously [2]. When using the method of regres-

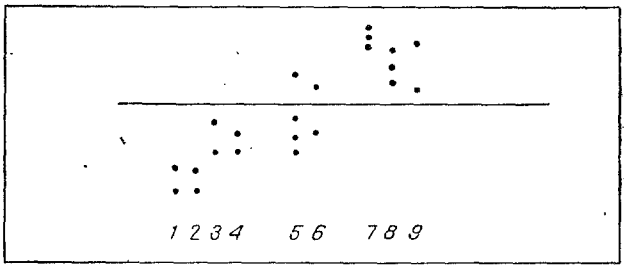

Fig. 1. Distribution of donors among groups of sensitivity to the antiproliferative action of dexamethasone. Position of dots along regression line determines type of sensitivity to which the donor belongs. Above the regression line – resistant type, below the line – sensitive type. Dots indicate results of single determinations, numbers are serial numbers of donors.

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TABLE 1. Parameters of Binding of GCH with Donors' Lymphocytes

No. of donor	Type of sensitivity	B_m, pM	K_d, nM	$(B_m/K_d) \times 10^{-3}$
1	Sensitive	34,81	5,0	6,96
2	»	63,29	5,5	11,51
3	»	19,62	3,1	6,33
4	»	22,78	3,0	7,59
5	Intermediate	15,19	2,5	6,08
6	»	40,51	4,9	8,27
7	Resistant	31,65	6,9	4,59
8	»	20,25	5,4	3,75
9	»	17,72	4,1	4,32

sion analysis two factors were included in the description of the type of sensitivity of the donors: the intensity of the proliferative response to PHA in a given experiment, expressed in ln cpm units, and the degree of inhibition of the proliferative response by dexamethasone, determined by the probit method, and expressed in the form log ED_{50}. Parameters of binding of GCH with lymphocytes were determined by the method described previously [3] by incubating a suspension of the test cells with ^{3}H-dexamethasone ("Amersham," Great Britain). The quantity of bound dexamethasone was calculated per liter of cell suspension in a concentration of 10^6 cells/ml. The maximal number of binding sites (B_m), the equilibrium dissociation constant (K_d), and also the index of efficiency of reception (B_m/K_d) were calculated [3]. To assess the significance of differences between the groups, the Wilcoxon–Mann–Whitney U test was used [1].

EXPERIMENTAL RESULTS

Determination of the types of sensitivity of lymphocytes from the nine donors studied showed that four donors could be classed as sensitive, three as resistant, and two as belonging to the intermediate type (Fig. 1). Comparison of the type of sensitivity of the lymphocytes both with the number of receptors for GCH (B_m) and with the dissociation constant (K_d) failed to reveal any form of correlation between them (Table 1). However, when an integral parameter such as the efficiency of reception (B_m/K_d) was introduced into the system of analysis, clearly the value of this parameter in the group of sensitive donors was much higher than in the group of resistant donors ($p < 0.05$).

The reason is that the method we used to assess the antiproliferative effect of GCH is based on the dose (concentration)–effect relationship, which in turn assumes that the effect depends both on the number of receptors (B_m) and on affinity of the hormone for the receptor (K_d).

Genetically determined parameters of binding of GCH with GCHR thus make an important contribution to the character of sensitivity of human lymphocytes to the antiproliferative action of GCH.

LITERATURE CITED

1. E. V. Gubler, Computational Methods of Analysis and Diagnosis of Pathological Processes [in Russina], Leningrad (1978).
2. E. A. Kalashnikova, L. A. Pukhal'skii, and L. A. Pevnitskii, Byull, Éksp. Biol. Med., No. 9, 334 (1988).
3. V. N. Lyashko and G. T. Sukhikh, Byull. Éksp. Biol. Med., No. 3, 273 (1987).
4. N. A. Mukhin, V. N. Lyashko, and K. N. Grinberg, Ter. Arkh., No. 5, 69 (1987).
5. F. Homo-Delarche, Cancer Res., 44, 431 (1984).
6. K. B. Walker, J. M. Potter, and A. K. House, Clin. Exp. Immunol., 68, 162 (1987).