DUAL CHARACTER OF INTERACTION BETWEEN LYMPHOCYTES AND ALLOGENEIC STEM CELLS

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In a study of interaction between mouse lymphocytes and allogeneic stem cells the writers found that the effect depends on the relative numbers of interacting cells [2]. Relatively large numbers of lymphocytes depress exogenous colony formation in the spleens of lethally irradiated recipient mice (the phenomenon of inactivation of allogenic stem cells [3]). A reduction in the number of lymphocytes injected, however, caused not simply the abolition of inactivation, but a marked stimulating effect — the number of macrocolonies was increased to twice or three times the control value.

In this investigation the mechanisms of stimulation of colony formation by small doses of allogeneic lymphocytes were studied.

EXPERIMENTAL METHODS

CBA mice were used in the experiments as donors, C57BL/6 mice were used as donors of bone marrow cells, and (CBA × C57BL/6)F_1 hybrids were used as recipients. Cell suspensions from LN and bone marrow were prepared by the usual methods.

When interaction of LN lymphocytes with allogeneic stem cells was studied, bone marrow cells ($0.3 \cdot 10^6$ per mouse) were injected into lethally irradiated recipients (800 R) in the control, and mixtures of bone marrow cells with varied numbers of LN lymphocytes were injected in the experiment.

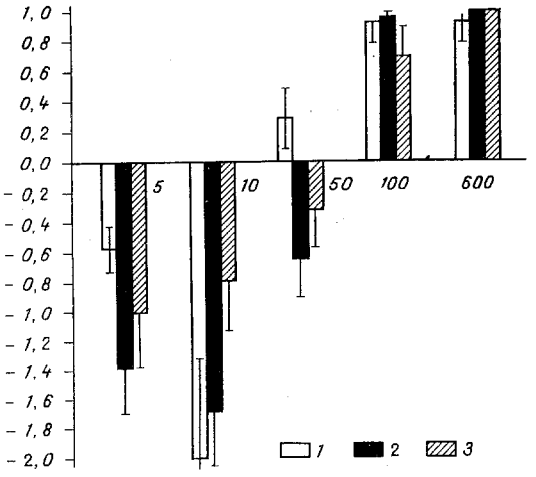

Fig. 1. Dependence of inactivation indices on number of lymphocytes injected (spleen). Abscissa, number of lymphotyces injected (in thousands per mouse); ordinate, inactivation index. 1) Macrocolonies in spleen on 11th day; 2) the same, on 8th day; 3) microcolonies (total number).

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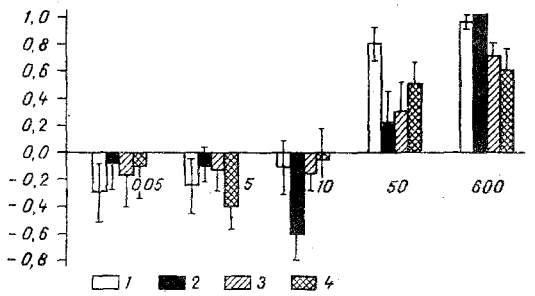

Fig. 2. Dependence of inactivation indices on number of lymphocytes (bone marrow) injected. 1) Erythroid microcolonies on 8th day; 2) the same on the 11th day; 3) myeloid microcolonies on 8th day; 4) the same on 11th day. Remainder of legend as to Fig. 1.

The number of colonies of CFU-S was counted on the 7th-8th day [6] and on the 11th day [5]. The number of macrocolonies in the spleen [6] was counted after removal of the spleens and their fixation in Bouin's fluid. Material (spleens, femora) was fixed in Bouin's solution and embedded in paraffin wax. Before embedding in wax, the bones were decalcified in 5% nitric acid. Histological sections 5-7 μ thick were cut with an interval of 150 μ. The sections were stained with hematoxylin and eosin. Microcolonies of erythroid and myeloid types were counted under the microscope. The quantitative characteristic of interaction between lymphocytes and allogeneic stem cells was the inactivation index:

$$I = \frac{S - S}{S},$$

where S denotes the mean number of colonies in the control group and S_e the same in the experimental group. Each group consisted of 10-12 animals.

The results were subjected to statistical analysis by the usual methods with certain modifications [1].

RESULTS

Dependence of the inactivation indices on the number of lymphocytes injected, based on the results of counting macro- and microcolonies in the spleen, is shown in Fig. 1. The inactivating action of relatively large numbers was replaced by distinct stimulation as the number of lymphocytes fell below 50,000 per mouse. The biphasic character of the interaction also was noted in the case of low-self-supporting CFU-S forming transient colonies on the 7th-8th day, and the high-self-supporting CFU-S, forming colonies on the 11th day.

Dependence of the inactivation indices after counting erythroid and myeloid microcolonies in the bone marrow on the 8th and 11th days is illustrated in Fig. 2. The general character of the change in the inactivation indices with a decrease in the number of LN lymphocytes was similar to that shown in Fig. 1. In precisely the same way relatively large numbers of lymphocytes caused inhibition of colony formation whereas small numbers of lymphocytes led to stimulation. Stimulation for both branches of hematopoiesis did not become significant until the 11th day.

It can be concluded from these results that stimulation of colony formation observed after injection of small numbers of lymphocytes is not connected with the redistribution of stem cells among the hematopoietic organs, but is evidently the result of involvement of additional stem cells which, in the control (in the absence of allogeneic lymphocytes), do not form colonies, in the process of colony formation.

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