DELIBERATE MODIFICATION OF THE SPECIFIC ACTIVITY OF LEUKEMIC CELLS

V. V. Parfenov, Yu. N. Tatarinova, and I. G. Balandin

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A comparative study was made of the efficacy of various types of deliberate modification of the leukemogenic activity of a transplantable line of bone marrow cells obtained from animals infected with Rauscher leukemia virus. Treatment of the leukemic cells with neuraminidase, or culturing them at a supraoptimal temperature led to complete loss of their leukemogenic activity, as shown by survival of 100% of the experimental animals and the absence of splenomegaly. Meanwhile, treatment of the cells with concanavalin A and 5-bromodeoxyuridine delayed the development of splenomegaly and lowered the mortality among the recipient animals by 70 and 20%, respectively. The results suggest that these methods of action on leukemogenic cells can be used in order to obtain material for subsequent immunization.

KEY WORDS: *leukemogenic cells; inhibition of specific activity.*

One of the most promising ways of controlling leukemia, it is generally considered, is by active immunization. There is thus no question about the urgency of the development of methods for acting upon leukemic cells in order to obtain highly effective immunizing material. Evidence has now been published that the oncogenic activity of tumor cells can be specifically depressed. This result has been achieved by various physical [2, 4], chemical [3, 5, 6], and biological [7] factors. However, the main disadvantage of investigations of this type has been that as a rule the effectiveness of only one procedure has been analyzed. Moreover, solid tumors have been used as the object of the procedure.

In the present investigation the effectiveness of various types of deliberate modification of the leukemogenic activity of a transplantable line of bone marrow cells obtained from animals infected with Rauscher leukemia virus was studied [1].

EXPERIMENTAL METHOD

The cells were treated once with *Vibrio cholerae* neuraminidase (Koch-Light Laboratories, England) for 0.5 h at 37°C in the proportion of 25 enzyme units/ml/10^6 cells. Treatment with concanavalin A (Sigma) lasted for 1 h at 37°C (50 μg/ml/10^6 cells). 5-Bromodeoxyuridine (Calbiochem, USA) was added to the culture medium (5 μg/ml) over the period of 20 subcultures. In the experiments to study the effect of a change in the cultivation temperature, the cells were first incubated for two subcultures at 39°C and then for 25 subcultures at 40.5°C. To determine the leukemogenic activity, cells treated as described above and also untreated cells (control) were injected intraperitoneally into BALB/c mice weighing 12-14 g in a dose of $2 \cdot 10^6$ cells per mouse. The experimental results were analyzed with respect to the development of splenomegaly and the survival rate of the mice after injection of the test cells.

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TABLE 1. Effect of Various Factors on Leukemogenic Activity of Transplantable Strain of Bone Marrow Cells Obtained from Leukemic Mice

Method of treatment	Time of appearance of splenomegaly, days	Survival rate of mice at period of observation indicated, days			
		14th	24th	30th	40th
Untreated cells (control)	10—14	9/10	7/10	4/10	0/10
Culture of 40.5°C	Not observed	10/10	10/10	10/10	10/10
Treatment with neuraminidase	Not observed	10/10	10/10	10/10	10/10
Treatment with concanavalin A	20—24	10/10	9/10	8/10	7/10
Treatment with 5-bromodeoxyuridine	18—20	10/10	8/10	5/10	2/10

Legend. Numerator gives number of mice surviving to indicated time of observation; denominator gives number of mice used in experiment.

As Table 1 shows, injection of bone marrow cells of leukemic mice led to the development of splenomegaly in the recipient animals (on the 10th-14th day), followed by death of all the mice. All types of procedures studied led to a decrease in the leukemogenic activity of cells of the transplantable bone marrow line, but the effect produced by physical factors was by no means uniform. For instance, treatment with concanavalin A and 5-bromodeoxyuridine delayed the development of splenomegaly and reduced the mortality among the recipient animals by 70 and 20%, respectively. Treatment of leukemic cells with neuraminidase, like cultivation at a supraoptimal temperature, led to total loss of leukemogenic activity, as was reflected not only in the survival of 100% of the experimental animals, but also in the absence of splenomegaly.

The results indicate that the most effective factors reducing the leukemogenic activity of the transplantable leukemic bone marrow cells were treatment with *V. cholerae* neuraminidase and culture at a supraoptimal temperature. On the basis of these results it is possible to contemplate the possible use of these methods of treatment of leukemogenic cells for the production of material for subsequent immunization.

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