INHIBITION OF GROWTH OF TUMOR Ca-755 IN MICE WITH RECONSTITUTED HEMATOPOIESIS

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Development and functional maturation of the immune system are controlled by factors produced by lymphoreticular cells. These factors play a central role in the production, development, and intensity of the immune response [3, 6, 7].

The varied course of responses of the immunologic system of the body, leading to differences in its effect on the development of the tumor process in vivo, is now evident. In particular, inhibition of tumor growth observed in thymectomized animals, subsequently irradiated and "protected" by embryonic liver cells (B mice), has been associated by some workers with depression of function of suppressor T cells, which play an important role in the mechanism of antitumor immunity [1, 2, 4, 5]. However, the data described in this paper are evidence of the existence of yet other factors inhibiting growth of a tumor (Ca-755), transplanted into mice two months after irradiation and protection by syngeneic bone marrow cells or by allogeneic fetal liver cells (AFL).

EXPERIMENTAL METHODS

Male (CBA × C57Bl/6j)F_1 mice (F_1), female SHK mice weighing 23-25 g, and pregnant BALB/c and SHK mice were obtained from the Stolbovaya and Kryukovo Nurseries. Suspensions of AFL and bone marrow cells were prepared in medium 199 with 10% fetal calf serum. The Ca-755 tumor was obtained from the Museum of Tumor Strains, All-Union Oncologic Scientific Center, Academy of Medical Sciences of the USSR. A 30% cell suspension was prepared in medium 199 and injected subcutaneously into the animals in a volume of 0.5 ml two months

TABLE 1. Time Course of Development of Tumor in Mice with Reconstituted Hematopoiesis

Recipient mice	Donor of hematopoietic cells (dose of protection)	Weight of tumor, g		
		10 days	14 days	18 days
F_1 Intact ($n = 10$)	—	1,4±0,10	2,7±0,16	6,9±0,62
F_1 Irradiated ($n = 10$)	F_1 Bone marrow ($10 \cdot 10^6$/0,5 ml)	0,17±0,04	0,56±0,11	1,9±0,28
F_1 Irradiated ($n = 7$)	BALB/c AFL ($40 \cdot 10^6$/0,5 ml)	0,19±0,59	0,41±0,09	1,59±0,25
SHK Intact ($n = 10$)	—	1,08±0,11	1,97±0,25	5,2±0,57
SHK Irradiated ($n = 8$)	SHK AFL ($40 \cdot 10^6$/0,5 ml)	0	0	0

Legend. Differences in size of tumors in all groups relative to intact control are statistically significant ($p < 0.001$).

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TABLE 2. Immunologic Reactivity of Mice after Irradiation and Transplantation of AFL Cells

SHK mice	Geometric mean HA titer, $\log_2$			Geometric mean AHA titer, $\log_2$		
	15 days	30 days	60 days	15 days	30 days	60 days
After irradiation and protection	0,57±0,35* (n=7)	4,6±0,21 (n=6)	5,2±0,51 (n=5)	7,0±0,33 (n=8)	6,8±0,6 (n=6)	7,2±0,47 (n=5)
Intact		5,14±0,56 (n=7)			7,0±0,92 (n=7)	

Legend. *$p < 0.001$ relative to all groups.

after transplantation of hematopoietic tissue. Transplantation of AFL and bone marrow cells was carried out on the day of irradiation of the animals on a ^{137}Cs radiation source in a dose of 10.5 Gy. On the 15th, 30th, and 60th day after irradiation and protection by AFL cells, the SHK mice (6 groups) were immunized with sheep red blood cells (SRBC) in a dose of $1.0 \cdot 10^8/0.5$ ml and with smallpox vaccine (SV) in a dose of 10^6 PFU/0.2 ml. Hemagglutinating (HA) and antihemagglutinating (AHA) antibodies were determined by a micromodification of the usual method in the sera of the mice 10 days after immunization with SRBC and 21 days after injection of SV. The weight of the neoplasm on the 10th and 14th days was expressed as the product of three perpendicular dimensions of the tumor multiplied by 2, and on the 18th day, as the weight of the tumor removed, in grams. The results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

Table 1 shows that growth of the Ca-755 tumor in mice with reconstituted hematopoiesis was strongly inhibited. This fact was observed in the group of animals protected after irradiation both by syngeneic bone marrow and by AFL cells. The Ca-755 tumors took and grew well in noninbred intact SHK mice and, at the same time, these animals were completely resistant to it after irradiation and transplantation of AFL cells. Transplantation of the tumor, incidentally, was carried out two months after transplantation of the hematopoietic tissue.

It will be clear from Table 2 that immunologic reactivity was depressed in SHK mice immunized with SRBC on the 15th day after irradiation and protection. On the 30th day it was restored and virtually indistinguishable from the control. Under these experimental conditions no differences were found in the titers of antihemagglutinating antibodies depending on the times of immunization of the mice with SV chosen.

The investigation thus revealed marked inhibition of growth of the Ca-755 tumor transplanted two months after reconstitution of hemtopoiesis in mice by syngeneic bone marrow cells and by AFL cells. Depression of immunologic reactivity of the mice to SRBC was observed on the 15th day after irradiation and protection with AFL cells.

Depression of growth of the Ca-755 tumor under these experimental conditions in the late stages after reconstitution of hematopoiesis is interesting from the point of view of the study of functional activity of different subpopulations of immunocompetent cells on transplantation of hematopoietic tissue into lethally irradiated animals.

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