COMPARATIVE IMMUNOGENICITY OF IRRADIATED AND NONIRRADIATED SYNGENEIC AND XENOGENEIC TUMOR CELLS CONTAINING A COMMON SPECIFIC TRANSPLANTATION ANTIGEN

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The immunogenic activity of native and irradiated syngeneic and xenogeneic tumor cells, carrying a common transplantation antigen specific for SV40 on their surface, was compared in Syrian hamsters. The results showed that syngeneic tumor cells were more immunogenic for the recipient than xenogeneic tumor cells containing antigen of the same specificity. Irradiation makes tumor cells, including xenogeneic cells, more immunogenic, possibly on account of the ability of the unirradiated cells to escape recognition on account of their ability to divide. KEY WORDS: tumor; specific transplantation antigen; immunogenic activity; irradiation.

Tumor cells are used most widely for specific immunization against tumors. The immunogenic activity of tumor cells has been shown to be influenced by several quantitative and qualitative factors: the antigenicity of the tumor cells, the size of the immunizing dose of cells, the mode of their administration, the sensitivity of the specific transplantation tumor antigen (STTA) on the cell membrane to various physicochemical factors [4-6]. However, problems such as the comparative immunogenicity of syngeneic and xenogeneic tumor cells containing a common STTA, and also the comparative immunogenicity of irradiated and unirradiated tumor cells have received little study. There is scattered information in the literature to show that tumor cells xenogeneic for the recipient are less immunogenic than syngeneic cells containing STTA of common specificity, and also some very contradictory information on the radiosensitivity of STTA in tumor cells belonging to different species [4-6].

Comparison of the immunogenic activity of native and irradiated tumor cells experimentally can be undertaken only if either cells xenogeneic for the recipients and transformed by the virus alone or cells of interspecific somatic hybrids carrying STTA on their surface, but incompatible with both parental species during transplantation are used for immunization.

In this investigation the immunogenic activity of xenogeneic native and irradiated mouse cells, transformed in vitro by SV40 virus, and cells of an interspecific somatic hybrid containing STTA specific for SV40 virus for Syrian hamsters was studied. Irradiated syngeneic cells of a tumor induced by SV40 virus in a Syrian hamster was used as the positive control.

EXPERIMENTAL METHOD AND RESULTS

The following cells were used to immunize the Syrian hamsters in the investigation: 1) irradiated cells of a culture of a syngeneic tumor (strain E-1) induced in a Syrian hamster by SV40 virus; 2) native and irradiated mouse cells from cultures of two strains, one of which was obtained in the writers' laboratory through transformation of a culture of kidney epithelial cells of a noninbred mouse by SV40 virus in vitro (strain MKTR) the other by transformation of a culture of embryonic fibroblasts of C57BL mice, transformed by the same virus (strain M-22); the latter strain was obtained in the Laboratory of Cytogenetics, Oncologic Scientific Center, Academy of Medical Sciences of the USSR, and was generously provided by A. A. Stavrovskaya;

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TABLE 1. Immunogenic Activity for Hamsters of Irradiated and Native Syngeneic and Xenogeneic Tumor Cells Containing STTA Specific for SV40 Virus (based on results of transplantation test)

Expt. No.	Immunizing material	No. of tumor cells injected	Irradiation	Results of transplantation test with test tumor SV40	
				log PD_{50}*	log IR†
1	Uninoculated control	—	—	1,50	—
	Hamster tumor cells (strain E-1)	$6 \cdot 10^6$	+	>3,50	>2,0
		$6 \cdot 10^5$	+	3,74	2,2
		$6 \cdot 10^4$	+	1,55	0,05
2	Uninoculated control	—	—	0,90	—
	Mouse cells transformed by SV40 (strain M-22)	$2,4 \cdot 10^8$	+	2,70	1,8
			—	1,0	0,1
		$1,2 \cdot 10^7$	+	0,70	0,2
			—	0,82	0,08
		$1,2 \cdot 10^6$	+	0,71	0,2
			—	1,20	0,3
		$1,2 \cdot 10^5$	+	0,95	0
			—	1,53	0,63
3	Uninoculated control	—	—	1,50	—
	Mouse cells transformed by SV40 (strain MKTR)	$5,5 \cdot 10^6$	+	2,88	1,38
			—	1,80	0,3
		$5,5 \cdot 10^5$	+	2,00	0,5
			—	2,20	0,7
		$5,5 \cdot 10^4$	+	2,20	0,7
			—	1,20	0

* Logarithm of 50% of dose of test tumor cells used to inoculate Syrian hamsters.

† Logarithm of index of resistance (difference between log PD_{50} in experiment and control).

TABLE 2. Immunogenic Activity of Native and Irradiated Cells of Interspecific Somatic Hybrid of Strain PZM-211 for Hamsters (based on results of transplantation test on Syrian hamsters)

Immunizing material	No. of cells injected	Irradiation in dose of 12,000 rad	Results of transplantation test with test tumor SV40*	
			log PD_{50}	log IR
Uninoculated control	—	—	1,7	—
Cells of interspecific somatic hybrid (strain PZM-211)	$2,2 \cdot 10^7$	—	⩾3,94	⩾2,27
		+	>4,7	>3,0
	$2,2 \cdot 10^6$	—	2,95	1,25
		+	>4,57	>2,87
	$2,2 \cdot 10^5$	—	2,2	0,5
		+	3,7	2,0

* Legend as in Table 1.

3) native and irradiated cells of an interspecific somatic hybrid of strain PZM-211 (hamster sarcoma induced by SV40 virus – normal kidney of a green African guenon), obtained in the writers' laboratory [1].

The test cells were removed from the glass with a solution of versene, counted, and half of them were irradiated in a dose of 10,000 rad on a Stebel'-3A Gamma-unit. The other half of the test cells was injected into hamsters in the native form. In all experiments hamsters were immunized once only, the material being injected intraperitoneally.

The immunogenic activity of the test tumor cells was verified after 14 days by the transplantation test in its most objective and sensitive modification [2], using as the test tumor a culture of hamster sarcoma cells induced by strain E-1 of SV40 virus.

The results of tests of the comparative immunogenic activity of irradiated cells of the syngeneic SV40

strain E-1 tumor and of native and irradiated xenogeneic mouse cells transformed by the same SV40 virus, for hamsters are shown in Table 1. The results in Table 1 show that irradiated cells of the syngeneic tumor of strain E-1 possessed high immunogenic activity: the minimal dose inducing resistance in these cells was $6 \cdot 10^5$ cells.

Injection of $2 \cdot 10^7$ unirradiated cells of strain M-22 and $5.5 \cdot 10^6$ cells of strain MKTR was insufficient to immunize the experimental hamsters against the syngeneic test tumor of strain E-1. However, the same doses of cells of both strains after irradiation induced definite antitumor immunity in the hamsters.

An increase in the immunogenic activity of the cells after irradiation also was found in the case of cells of the interspecific somatic hybrid of strain PZM-211, containing STTA specific for SV40 virus (Table 2).

The minimal immunizing dose of cells, which was $2 \cdot 10^6$ for unirradiated PZM-211 cells, was 10 times less ($2.2 \cdot 10^5$) for irradiated cells.

It can thus be concluded from the results that xenogeneic tumor cells, injected into a recipient, other conditions being the same, are much less immunogenic than cells of a syngeneic tumor containing STTA of the same specificity. This phenomenon may perhaps be connected with differences in the recognition of STTA by the host on injection of xenogeneic and syngeneic tumor cells. This suggestion is confirmed by the experimental data showing differences in the cytotoxic reaction of T-lymphocytes to antigens present on the membrane of syngeneic and xenogeneic cells infected with influenza virus of the same serotype [3].

Irradiation (10,000 rad) also makes tumor cells more immunogenic for the recipients. It can tentatively be suggested that unirradiated (including xenogeneic) tumor cells evidently have the ability to escape recognition, a property which may perhaps be connected with their mitotic activity.

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