Inhibition of ^{3}H-L incorporation in the presence of LO from *Tr. harzianum* Rifai was not significant, and the highest value of inhibition was obtained after incubation for 24 h (Fig. 2c).

The final values of inhibition of DNA and RNA synthesis in the presence of enzymes from the two sources was shown to be virtually a linear function of enzyme concentration (Fig. 3a, b).

Preparations of LO from the Soviet producer strain of *Trichoderma harzianum* Rifai and from the Japanese strain *Trichoderma viride* Y244-2* thus has a similar inhibiting action on the processes studied.

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CHANGES IN ANTITUMOR RESISTANCE OF HAMSTERS FOLLOWING EXPERIMENTAL REMOVAL OF UNFIXED MACROPHAGES

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UDC 616-006-092.19:616.1.155.33-033.1

KEY WORDS: antitumor resistance; peritoneal exudate; macrophages.

Many investigations have demonstrated the important role of macrophages in the development of resistance to tumors [1-3, 5, 7]. The mechanisms by which macrophages kill human cells are not clear. However, direct contact between effector macrophages and target cells is probably necessary. The number of macrophages in the tissue of a growing tumor is known to correlate negatively with the formation of spontaneous metastases [6, 8]. It is accordingly natural to suppose that experimental removal of mobile macrophages (and other effector cells interacting with macrophages) from the location of tumor cells could significantly modify the antitumor resistance of the animal.

The aim of this investigation was to test this hypothesis.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred Syrian hamsters reared at the "Stolbovaya" nursery, Academy of Medical Sciences of the USSR. Transplantable sarcoma Ad-12, induced initially in hamsters by human type 12 adenovirus, was used as the test tumor. The transplantation test was used in Murka's modification [4]. Hamsters of the experimental and control groups were inoculated subcutaneously with sarcoma Ad-12 cells at four points of their body in the following doses: 10^2, $2 \cdot 10^2$, 10^3, and 10^4. The experimental results were assessed by means of the following parameters: the latent period of appearance of tumors and the percentages of positive inoculations.

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(Presented by Academician of the Academy of Medical Sciences of the USSR S. N. Khechinashvili.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 103, No. 4, pp. 460-462, April, 1987. Original article submitted January 28, 1986.

TABLE 1. Cell Composition (in %) of Peritoneal Exudate of Hamsters at Various Times after Injection of 3% Starch Suspension

Time of investigation after injection of starch, h	Macrophages	Neutrophils	Monocytes	Lymphocytes
Control	15,5	7,0	16,0	61,5
(n=10)	(8,5—21,0)	(1,0—19,0)	(10,5—23,0)	(52,0—71,0)
1	21,0	13,0	5,0	61,0
(n=10)	(13,0—26,0)	(10,0—18,0)	(3,0—12,0)	(49,0—69,0)
24	41,0	4,5	19,0	34,5
(n=10)	(19,0—58,0)	(1,6—6,0)	(12,0—32,0)	(18,0—55,0)
48	27,0	1,0	15,0	56,0
(n=5)	(12,0—35,0)	(0—2,0)	(8,0—28,0)	(44,0—70,0)

Legend. Limits of variations indicated between parentheses.

TABLE 2. Stimulation of Growth of Adenovirus-Induced Tumor in Hamsters after Removal of Mobile Macrophages into the Peritoneal Cavity

Group of animals	Fraction of inoculated tumor cells	Latent period, days	Percent of successful inoculations
Control	10^2	—	0
	$2 \cdot 10^2$	—	0
	10^3	29,0±1,0	52
	10^4	19,0±2,6	100
Experiment	10^2	32,6±1,8	53
	$2 \cdot 10^2$	29,6±2,2	72
	10^3	23,4±1,6	90*
	10^4	16,0±2,6	100

Legend. Mean results of five series of experiments are given. *$p < 0.01$.

A 3% suspension of starch, injected intraperitoneally into hamsters of the experimental group, was used as the agent to remove mobile macrophages from the location of the tumor cells; intact animals served as the control. To determine the nature of the response of the hamsters to intravenously injected irritant, the peritoneal exudate was tested at various times after injection of the starch suspension: 1, 24, and 48 h. For the cytological investigation peritoneal exudate cells were obtained by irrigating the peritoneal cavity of the animals with Hanks' solution with the addition of 10% bovine serum. The cells were sedimented by centrifugation in the cold at 1000 rpm for 5 min. Films were made from the residue, fixed in 96° alcohol, and stained by Romanovsky's method.

The Wilcoxon—Mann—Whitney test was used to assess the significance of differences between data in the experimental and control series.

EXPERIMENTAL RESULTS

Lymphocytes predominated in the peritoneal exudate of intact hamsters (Table 1). Exudate with the largest number of monocytes (12-32%) and macrophages (19-58%) was formed in the peritoneal cavity 24 h after injection of the irritant. Consequently, by this time the phagocytic activity of the lymphoid-macrophagal cells in the hamsters' peritoneal cavity was at its peak. For that reason, the injection of 2 ml of 3% starch suspension was given intraperitoneally to the animals 24 h before transplantation of the tumor cells.

It will be clear from the data in Table 2 that the latent period of onset of tumors in animals receiving starch before subcutaneous transplantation of 10^3 and 10^4 malignant cells (threshold doses) was considerably shorter than in animals of the control group. Differences between the frequency of appearance of tumors in animals of the experimental (90%) and control (52%) groups after transplantation of 10^3 tumor cells were statistically significant.

However, differences between the frequency of appearance of tumors in the experimental and control animals were more significant after transplantation of small numbers of tumor cells. For instance, in hamsters of the control group no tumors arose after subcutaneous

transplantation of sarcoma Ad-12 cells in doses of 10^2 and 2×10^2, whereas in hamsters of the experimental group (receiving a preliminary injection of starch suspension) tumors appeared in 53-72% of cases after transplantation of the same numbers of malignant cells (the stimulation of tumor growth phenomenon). Thus, animals naturally resistant to small numbers of tumor cells, after appropriate treatment become sensitive to inoculation with these cells.

The results of this investiation are evidence that the appearance of tumors in hamster after subcutaneous transplantation of small doses (10^2, $2 \cdot 10^2$) of Sarcoma Ad-12 cells after preliminary injection of starch suspension is associated with removal of mobile macrophages from the location of tumor cells into the peritoneal cavity..

Local or general mechanisms through which tumor growth is stimulated are not yet known, and may be various. However, there is no doubt that after removal of mobile macrophages, the primary antitumor resistance of the animal may be modified. Consequently, an essential role in the effective proteetion of the organism against small numbers of tumor cells is played by nonspecific resistance, which may be effected through macrophages.

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EXPRESSION OF VIMENTIN AND PREKERATINS IN SOLID AND ASCITES VARIANTS OF ZAJDELA's HEPATOMA

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UDC 616.36-006-008.939.6-092.18

KEY WORDS: intermediate filaments; hepatoma; intercellular junctions; extracellular matrix.

Cells of various tissues contain intermediate filaments (IF) consisting of subunits specific for the given type of tissue [9]. Primary and transplantable epithelial tumors, including liver tumors, still contain IF proteins characteristic of epithelium, namely prekeratins (PK), and they do not express the IF protein specific for connective tissue, namely vimentin [4, 7]. The only exceptions are certain forms of carcinomas of the salivary glands and kidneys [6, 12]. By contrast with this, besides PK, as a rule vimentin filaments also are found in ascites forms of carcinoma [10]. The reasons for this anomalous expression of vimentin in ascites forms of carcinoma are not known. The solution to this problem must be found before we can understand the mechanisms both of normal morphogenesis and of the disturbances of morphogenetic processes in tumor growth.

EXPERIMENTAL METHOD

Zajdela's ascites hepatoma (ZAH), obtained from the Collection of Tumor Strains, All-Union Oncologic Scientific Center, Academy of Medical Sciences of the USSR, was transplanted intraperitoneally into adult noninbred male rats. The transplantation was repeated every 5

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 103, No. 4, pp. 462-466, April, 1987. Original article submitted June 12, 1986.