ANTIGENIC PROPERTIES OF HUMAN TUMOR AND EMBRYONIC TISSUES

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The cells of malignant tumors are very similar to embryonic cells both morphologically and with respect to some aspects of their chemical composition and metabolism. Immunological investigations of these tissues [3, 4, 13-15] have demonstrated the similarity of their antigenic composition.

Reports have recently been published [1, 2] that the antigen of the transplantable hepatoma of mice (strain XXIIa) is identical with embryonic serum α-globulin. This antigen is present in the serum and liver of mouse embryos but absent from the blood and organs of adult animals, and it is actively synthesized by the hepatoma.

Embryonic α-globulin has also been found in the serum of a patient with primary hepatocellular carcinoma of the liver [11].

These discoveries evidently do not constitute a general rule for all patients with carcinoma and all animals with tumors. For instance, embryonic α-globulin is not found [1, 2] in mice with Ehrlich's carcinoma, with Cracker's sarcoma, and with some forms of transplantable hepatomas (strain XXII). Embryonic α-globulin was not found [11] in the sera of patients with carcinoma of the esophagus, stomach, and intestine, and also of patients with metastases of a carcinoma in the liver.

On the other hand, results have been obtained demonstrating antigenic differences between embryonic and tumor tissues in rats [12], and also between human patients with carcinoma of the stomach and leukemia [9, 10].

The object of the present investigation was to compare the specific antigenic properties of human carcinoma and embryonic tissues, using for this purpose methods of immunological analysis of tissues developed in the author's laboratory.

EXPERIMENTAL METHOD

The material used for the study consisted of the tissues of malignant tumors, of human embryos aged 6 weeks, and also tissue from the spleen of healthy adults after accidental death.

The method of obtaining heteroimmune tumor and organ-specific antisera, and the technique of performing the complement fixation reaction and the specific absorption used in this investigation were described by the authors in earlier communications [5-7].

The antigens used were saline extracts from the tumors and from the spleen of the adult subjects, the liver, kidneys, skeletal muscles, heart, and lungs of embryos, and also antigens from mixtures of embryonic tissues including the spleen.

Since the specific antigens of tumors, in contrast in certain organ-specific antigens, are readily soluble in alcohol, besides antigens from native tissues, emulsions (in physiological saline) of alcoholic extracts of the tumors were also tested. By means of ethyl alcohol an attempt was also made to extract antigenic substances from the embryonic tissues and to compare them with the tumor antigens.

For control purposes a standard Wasserman antigen – an alcoholic extract of beef heart – was tested.

EXPERIMENTAL RESULTS

The results of one of the typical and frequently reproducible experiments to compare the reaction of antigens from adult and embryonic tissues with tumor antiserum No. 104, obtained by immunization with

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Comparative Study of Antigens from Human Tumor and Embryonic Tissues in the Complement Fixations and Specific Absorption Reaction

Immune serum	Tissue used for absorption of serum	Dilution of serum	Antigens										
			From native adult tissues		From native embryonic tissues						Alcoholic extracts		
			Tumor of patient S.	Spleen	Mixture of tissues	Liver	Kidney	Muscles	Heart	Lungs	Tumor of patient S.	Mixture of embryonic tissues	Wassermann antigens
No. 104 (against a metastasis of carcinoma of the rectum in the liver of patient S.)	Before absorption	1:80	++++	++++	++++	++++	+++	++++	++++	+++	++++	—	—
		1:160	++++	+++	+++	+	++	+++	+++	+	++++	—	—
		1:320	++++	++	++	—	+	+	++	—	++++	—	—
		1:640	++++	+	+	—	—	—	+	—	++++	—	—
	Formalinized healthy human spleen	1:80	++++	—	—	—	—	—	—	—	++++	—	—
		1:160	++++	—	—	—	—	—	—	—	++++	—	—
		1:320	+++	—	—	—	—	—	—	—	+++	—	—
		1:640	+	—	—	—	—	—	—	—	+++	—	—
	Formalinized tumor of patient S.	1:80	—	—	—	—	—	—	—	—	—	—	—
		1:160	—	—	—	—	—	—	—	—	—	—	—
		1:320	—	—	—	—	—	—	—	—	—	—	—
		1:640	—	—	—	—	—	—	—	—	—	—	—
	Mixture of native embryonic tissues	1:80	++++	—	—	—	—	—	—	—	++++	—	—
		1:160	++++	—	—	—	—	—	—	—	++++	—	—
		1:320	+++	—	—	—	—	—	—	—	+++	—	—
		1:640	+	—	—	—	—	—	—	—	+++	—	—
No. 117 (against human healthy spleen	Foramalinized healthy human liver	1:40	—	++++	+++	—	—	—	—	—	—	—	—
		1:80	—	++++	+	—	—	—	—	—	—	—	—
		1:160	—	+++	—	—	—	—	—	—	—	—	—
		1:320	—	+	—	—	—	—	—	—	—	—	—

Legend: ++++, +++, ++, + different degrees of positive complement fixation reaction; —negative reaction.

native antigen from a tumor present in patient S., and with organ-specific serum No. 117 against healthy human spleen are given in the table.

It is clear from the table that the heteroimmune tumor antiserum reacted both with antigen from the native tumor and the alcoholic extract from it, and also with native antigens from the embryonic tissues, demonstrating their antigenic similarity with the tumor tissue. However, the intensity of this reaction with antigens from embryonic tissues was no higher than that with the extract from the healthy human spleen.

After absorption of equal volumes of tumor antiserum No. 104 with the same quantity of healthy adult spleen tissue, tumor tissue, and embryonic tissue and subsequent testing of these sera in the complement fixation reaction, the following results were obtained. As described in a previous communication [6], absorption of the serum with spleen tissue made it specific. The serum absorbed in this way reacted only with antigens from the tumor and did not react with antigens from the adult human spleen. As the table shows, this serum did not react either with antigens from the embryonic tissues.

Consequently, the antigenic similarity between human tumor and embryonic tissue discovered in experiments with unabsorbed serum is due to nonspecific antigens common both to tumor and embryonic tissues. The results of the reaction obtained with a specific tumor antiserum demonstrated qualitative differences between human tumor and embryonic tissues.

This was confirmed also by experiments on absorption of the serum by tumor and embryonic tissues. It is clear from the table that the tumor cells absorbed all the antibodies from the serum, after which it failed to react with any of the antigens used in the experiment. Meanwhile, absorption of another portion of this serum by embryonic tissues did not remove the tumor antibodies from the serum, and such a serum, when absorbed by the embryonic tissues, could still fix complement in the presence of saline and alcoholic extracts of the tumor. In the absorption experiments, the embryonic tissue thus behaved like adult human spleen.

The specificity of the reaction may be assessed by cross-testing the antigens with an organ-specific antiserum against human spleen, giving a positive reaction only with antigens from the spleen and with a mixture of embryonic tissue including embryonic spleen, and also from the negative reaction of the sera with heterogenic Wasserman antigen.

The results given in the table also reveal differences in the behavior of the human tumor and embryonic tissues toward ethyl alcohol. Whereas the tumor antigen was soluble in this organic solvent and the alcoholic extract of the tumor possessed specific antigenic activity, the analogous antigen from the mixture of embryonic tissues did not possess serological activity and did not react even with unabsorbed tumor antiserum. In their insolubility in ethyl alcohol, the embryonic antigens were similar to human organ-specific antigens [8].

This investigation of the antigenic properties of malignant and embryonic tissues thus demonstrates qualitative differences between them, i.e., that human tumors contain specific antigens not found in either adult or embryonic human species. Consequently, human cancer cells are not immunologically identical with embryonic cells, despite their morphological, biochemical, and to some extent, their antigenic similarity.

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