other tumors contained only small amounts of these proteins. Divergent anaplasia also was exhibited in the group of glioblastomas.

The results indicate the need for combined determination of several specific markers and they demonstrate the advantage of immunochemical determination of protein D_2 over that of proteins S-100 and GFAP in the differential diagnosis of malignant brain tumors.

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STRAINS OF TUMORS OF THE HUMAN GASTROINTESTINAL TRACT AND UTERUS TRANSPLANTABLE INTO NUDE MICE AND RATS

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KEY WORDS: human tumors; nude mice and rats.

Nude mice or rats are nowadays used as experimental models of human tumors. Transplantation of human tumors into nude mice has been carried out on quite a wide scale since 1969 [5]. Recently papers have been published on heterografting of human tumors into nude rats also [1-6].

In the investigation described below 30 strains of human tumors transplantable into nude mice and 30 strains transplantable into nude rats were obtained. It is therefore possible to study the same human tumor in different laboratory animals. The strains obtained will be described in a series of communications. This paper describes strains of carcinoma of the colon (RTK-1, RTK-2, RTK-7), carcinoma of the stomach (RZh), chorionepithelioma of the uterus (KhÉ), carcinoma of the cervix uteri (RShM), and carcinoma of the body of the uterus (RTM), transplantable into nude mice and rats.

EXPERIMENTAL METHOD

Nude mice were used at the age of 6-8 weeks and nude rats at the age of 4-6 weeks respectively. Human tumors used for transplantation were obtained during surgical operations. The tumors were transplanted subcutaneously in fragments into the mice. Strains RTK-1, RTK-2, RTK-7, RZh, KhÉ, and RTM were obtained in this way. Strain RShM was obtained by transplanta-

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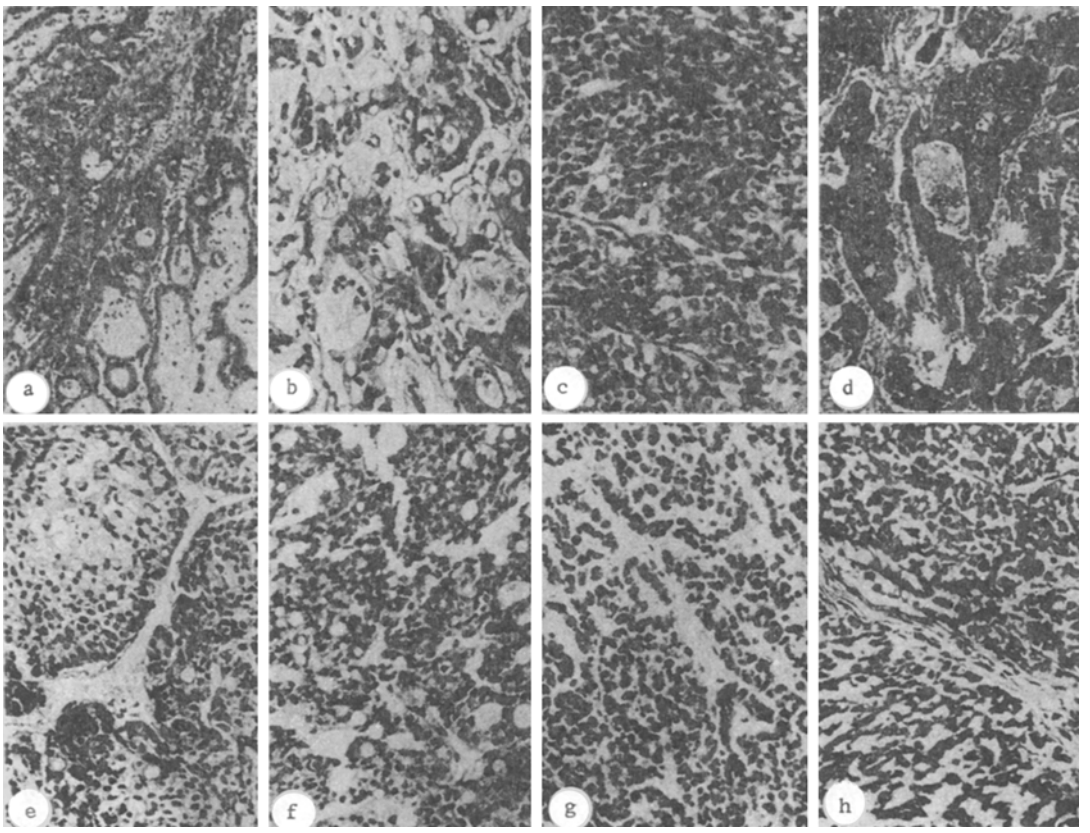

Fig. 1. Morphologic picture of tumor: a) original tumor for strain TRK-1, an adenocarcinoma of the colon with mucus production; b) strain RTK-1, 7th generation, an adenocarcinoma with mucus production; c) strain RTK-1, 78th generation, adenocarcinoma with low degree of differentiation; d) original tumor for strain RTK-2, an alveolar-solid carcinoma with mucus production; e) strain RTK-2, 8th generation, an alveolar-solid carcinoma with intracellular mucus production; f) strain RTK-2, 56th generation, mucous carcinoma; g) strain RTK-7, 8th generation, adenocarcinoma with low degree of differentiation; h) strain RTK-7, 45th generation, adenocarcinoma with low degree of differentiation and with areas of solid structure. Hematoxylin-eosin. Magnification: a, d) 63×; b, c, e-h) 160×.

tion of cell line HeLa of carcinoma of the cervix uteri, maintained in tissue culture. In this case the mice were inoculated subcutaneously with 0.5 ml of medium containing 10^6 cells. Subsequent serial transplantations in mice were performed subcutaneously with suspension containing 150 mg of tumor tissue in 0.5 ml. The same suspension from human tumors, after preliminary serial passage in mice, was injected into rats. A cell suspension also was used for some serial transplantations into rats. To determine the histological characteristics of the tumors sections were stained with hematoxylin and eosin, picofuchsine, and by the PAS reaction. To determine the species-specificity of the human tumor strain transplanted into nude mice and rats, the method of lactate dehydrogenase (LDH) electrophoresis in agar gel was used.

EXPERIMENTAL RESULTS

Strain RTK-1 has undergone continuous passage in 79 generations from 1976 through 1984 (i.e., for 8 years) with intervals of 15-18 days between transplantation. The tumor preserves in principle the structure of an adenocarcinoma with intracellular and intercellular production of mucus. During passage the degree of tissue differentiation has somewhat diminished. Whereas in the original tumor from the patient (Fig. 1a) and in the first passage it was an adenocarcinoma with an average degree of differentiation (Fig. 1b), the 78th generation is described as an adenocarcinoma of average and low degree of differentiation, with high mitotic activity (Fig. 1c).

Strain RTK-2, the original tumor with which was an adenocarcinoma (Fig. 1d), like RTK-1, has been maintained by passage with intervals of 15-18 days from 1976 until the present time.

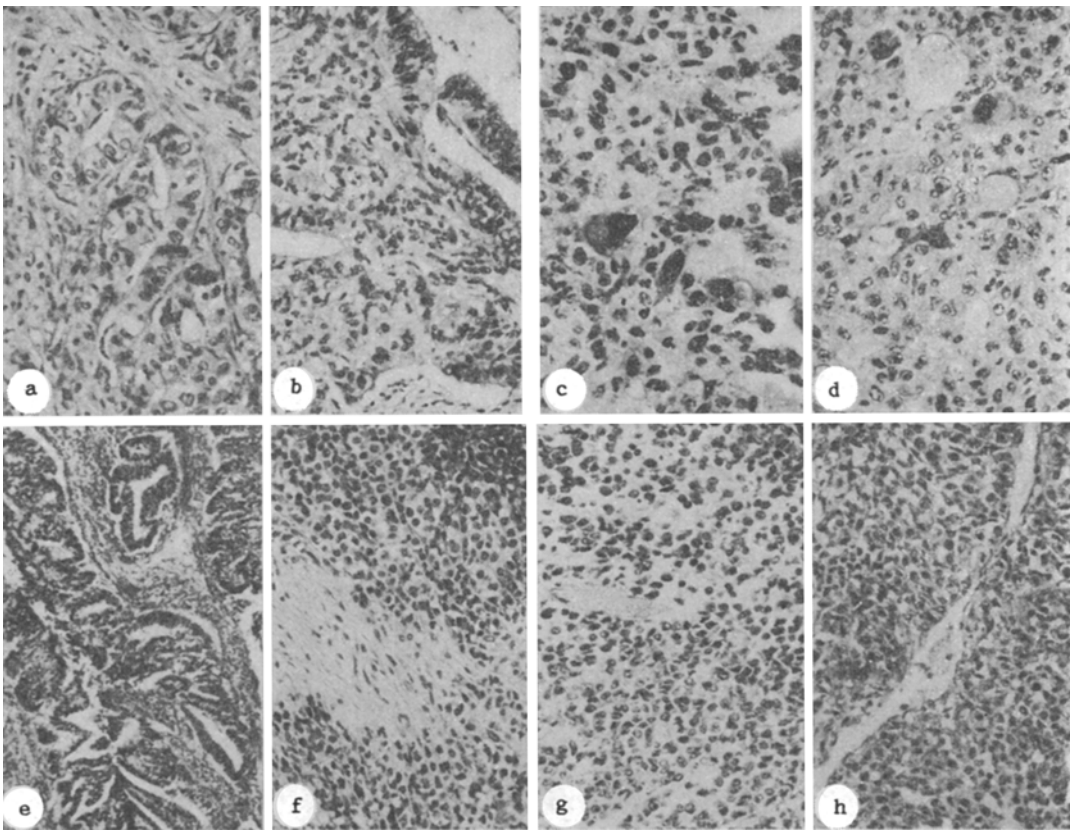

Fig. 2. Morphological picture of tumor: a) original tumor for strain RZh, an adenocarcinoma of the stomach; b) strain RZh, 43rd generation, adenocarcinoma; c) original tumor for strain KhÉ, chorionepithelioma of the uterus; d) strain KhÉ 67th generation, chorionepithelioma; e) original tumor for strain RTM, adenocarinoma of the body of the uterus; f) original tumor for strain RTM, carcinoma of the body of the uterus with a low degree of differentiation; g) strain RTM, 27th generation, carcinoma with a low level of differentiation; h) strain RShM, 16th generation, nonkeratinizing squamous-cell carcinoma. a-c, e-h) Hematoxylin-eosin; d) picrofuchsine. Magnification: a-d, f-h) 160×; e) 63×.

Under these circumstances it has preserved a sufficiently stereotyped structure with the formation of alveolar-gladular complexes of different sizes and with well-marked ability to form mucus (Fig. 1e, f).

Strain RTK-7, maintained by passage every 15-18 days, has the structure of an adenocarcinoma with a low degree of differentiation and with regions of mucous, and sometimes of signet-cell structure (Fig. 1g). Starting with the 44th generation, besides the structure of an adenocarcinoma, solid regions also have appeared. By the 67th generation the tumor preserved the structure of an adenocarcinoma with a low degree of differentiation, but formed solid regions of large size (Fig. 1h).

The original tumor for strain RZh was an adenocarcinoma of the stomach with average degree of anaplasia (Fig. 2a). The strain has been subcultured at intervals of 30-34 days, and has undergone continuous passage for 8 years from 1976 through 1984, during which it has preserved the structure of an adenocarcinoma with the production of small quantities of mucus, and has acquired some degree of structural monomorphism (Fig. 2b). Strain KhÉ has been subcultured since 1977 at intervals of 14-17 days and has not gone through 97 passages. It still preserves the structure of the original tumor, characteristic of a chorionepithelioma of the uterus, with some features of marked polymorphism of the chorionic epithelium, with distinct manifestations of fibrinoid necrosis, with massive hemorrhages, and with free circulation of blood cells in the tumor tissue and numerous atypical mitotic figures in the cells of the chorionic epithelium. Proliferation of areas of cells of Langhans' layer is present (Fig. 2c, d). Strain TRM has been subcultured since January 1983 at intervals of 7-8 days, and has gone through 60 passages. The original material for it was a uterine tumor with dimorphic

structure of adenocarcinoma and carcinoma with a low degree of differentiation (Fig. 2e, f). Throughout the period of passage the tumor has preserved in principle a stereotyped structure and cell composition and has corresponded to the picture of a carcinoma with low degree of differentiation. Features of glandular structure (adenocarcinoma), observed in the original material, could not be detected in any of the generations studied (Fig. 2d). Strain RShM, serially transplanted into animals at intervals of 14-15 days, preserved the structure of a nonkeratinizing squamous-cell carcinoma, corresponding to the original tumor from which the HeLa cell line, which was the source of the strain, was obtained (Fig. 2h).

All 14 tumors strains described in this communication, which were transplantable into nude mice and rats, consisted mainly of human cells, as shown by LDH electrophoresis, revealing five peaks.

Strains transplantable into nude mice and rats and obtained from the same human tumor were histologically identical with one another. However, stromal cells of strains transplanted into mice and rats differed, for they consisted of cells of the tumor-bearing host. With the models obtained it is possible to study human tumors under different experimental conditions and they enable transplantable tumors, especially from rats, in which they attain a large size, to be used for biotechnological purposes.

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EFFECT OF ANTICARCINOGENS ON THE TRANSPLACENTAL CARCINOGENIC EFFECT OF N-NITROSO-N-ETHYLUREA

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The study of the effect of various modifying factors on carcinogenesis is one approach to the elucidation of the pathogenetic mechanicsms of development of tumors and the devising of measures of their prevention. We know that tumors in children, and sometimes even in adults, may be due to the action of carcinogens on the mother during pregnancy [1]. Consequently, experimental data on the effect of anticarcinogens on the realization of transplacental carcinogenesis must be taken into account when measures are devised for preventing prenatally induced neoplasms in man.

In this investigation the action of seven different anticarcinogeneic agents was studied on the development of tumors of the nervous system and kidneys induced transplancentally in rats by N-nitroso-N-ethylurea (NEU). The choice of substances was dictated by the need for the agents used to have an anticarcinogenic action when given to the progeny only in the postnatal period, which is a model of the most suitable approaches for inhibiting prenatally induced neoplasms in man. For this purpose the known inhibitors of carcinogenesis — selenium [8] and vitamin A [11] — were used. Low-molecular-weight polypeptide factors obtained from tissue extracts of the bovine thymus, pineal gland, and bone marrow, acting on the immune and

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