HUMAN COLONIC CANCER STRAINS TRANSPLANTABLE INTO NUDE MICE AND RATS

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Malignant tumors of the human colon are transplanted most successfully into nude mice and rats [1, 3, 4]. Serial transplantation in nude animals has enabled human colonic cancer strains to be obtained. This paper describes five such strains, the original material for which consisted of tumors taken from patients during operations in the clinic of the All-Union Oncologic Scientific Center, Academy of Medical Sciences of the USSR.

EXPERIMENTAL METHOD

Nude mice based on line BALB/c aged 6-8 weeks and nude rats aged 4-6 weeks reared by ourselves were used. Immediately after removal from the patients the tumors were transplanted subcutaneously in fragments into the animals. Tumors were transplanted into rats after serial passage through nude mice in a suspension of 0.5 ml containing about 150 mg of tumor tissue. After the second passage, serial passage in both mice and rats was effected with tumor suspension.

The species of the transplanted strains was determined by electrophoresis of lactate dehydrogenase in agar gel.

To determine the histological characteristics of the tumors, sections were stained with hematoxylin and eosin, picrofuchsine, and by the PAS reaction.

EXPERIMENTAL RESULTS

Three transplantable strains of colonic cancer RTK-9, RTK-10, and RTK-12 were obtained from metastases in lymph nodes of different patients, and two other strains were obtained from the same patient: RTK-11 (p) from the primary tumor and RTK-11 (m) from a metastasis. All the strains were transplanted from one animal to another at intervals of 14 days. The rate of growth of tumors in the rats was much faster than in mice, and the tumors in rats after 14 days were much larger (by 10-15 times). All the strains obtained corresponded in histologic characteristics to tumors which were their original source.

Strain RTK-9 preserved the structure of the original tumor for 42 passages (Fig. 1a). This strain is a mucous adenocarcinoma. The lumina of the glands were distended by large quantities of mucus material, in some areas with compression and atrophy of the epithelium (Fig. 1b).

The original tumor for strain RTK-10 was a metastasis of an undifferentiated "signet-cell" carcinoma (Fig. 1c). This strain has passed through 31 passages and in the course of serial transplantations it preserved the structure of a "signet-cell" carcinoma with small areas of adenocarcinoma, which was distinguished by high mucus production (PAS-positive) (Fig. 1b).

Strain RTK-11 (p) and RTK-11 (m) are similar in histologic structure and are adenocarcinomas with high mucus production (Fig. 1e, f), corresponding to the picture of the patient's primary tumor.

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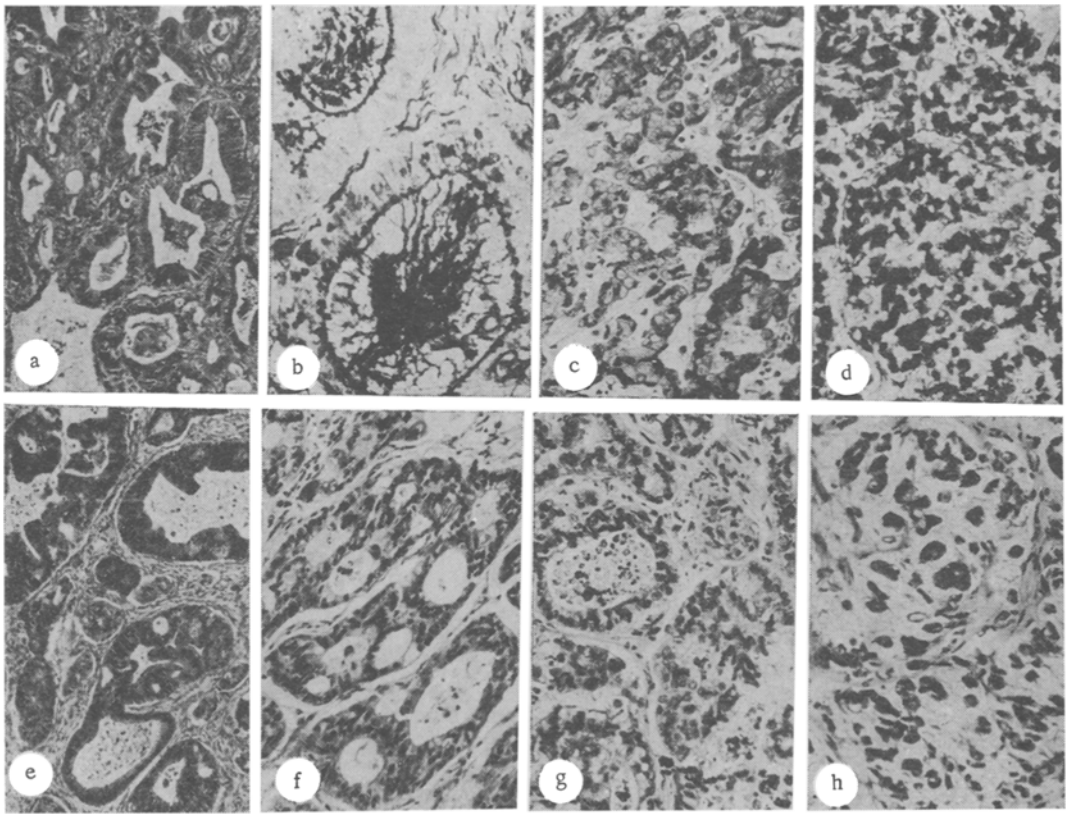

Fig. 1. Strains of human colonic cancer. a) Original tumor for strain RTK-9, an adenocarcinoma of the colon with high mucus production; e) RTK-11 (p), an adenocarcinoma of the large intestine. b) Strain RTK-9 of colonic carcinoma, 29th generation, adenocarcinoma with high mucus production; c) RTK-10, 18th generation, an adenocarcinoma with elements of "signet-cell" carcinoma and with high mucus production; d) RTK-10, 18th generation, an adenocarcinoma with elements of "signet-cell" cancer and high intracellular mucus production; f) RTK-11 (p), 2nd generation, adenocarcinoma; g) RTK-11 (m), 1st generation, adenocarcinoma; h) RTK-12; 1st generation, adenocarcinoma with high mucus production. a, c, e-h) Hematoxylin and eosin; b, d) PAS reaction; magnification: a, e) 63×; b-d, f-h) 160×.

Strain RTK-12 corresponds to the original tumor from which it was obtained, namely an adenocarcinoma with elements of "signet-cell" carcinoma and with high mucus production (Fig. 1g, h).

All five strains obtained, when transplanted into nude animals, consisted mainly of human cells. This is shown by the distribution of lactate dehydrogenase isozymes during electrophoresis. Lactate dehydrogenase from these five strains has five peaks, which is characteristic of human cells, and not one peak, which corresponds to mouse cells, or two peaks, which corresponds to rat cells.

The strains described above can be used as the source for obtaining carcinoembryonic and other tumor antigens. This is particularly true of tumors transplanted in rats, for they attain a large size. Strains of human colonic cancer transplanted into nude animals can also provide a convenient model with which to develop methods of early diagnosis of tumors [2].

The available set of strains can also be used to assess objectively the various methods of treatment of human colonic cancer, for the use of several strains cancels out differences in individual sensitivity of the tumors to therapeutic procedures such as chemotherapeutic agents, hormones, and irradiation.

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CELL STRUCTURE AND PROLIFERATIVE ACTIVITY OF ORGAN CULTURES OF NORMAL EMBRYONIC LUNG TISSUE OF MICE RESISTANT (C57BL) AND PREDISPOSED (A) TO LUNG TUMORS

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Mice of lines A and C57BL differ in being predisposed and resistant respectively to spontaneous and induced carcinogenesis of the lung [1, 10]. Interlinear differences in sensitivity of mice to pulmonotropic carcinogens are known to be manifested as early as during prenatal ontogeny and they persist in isolated lung tissue when explanted in organ culture [3-5, 9, 10]. It has been found that the ability of organ cultures of normal embryonic lungs of A mice to survive is significantly less than that of C57BL mice [3-5]. Among the many factors influencing realization of carcinogenic effects the most important, as we know, are the degree of differentiation and the proliferative activity of cells in target organs [15]. This, in particular, explains the high sensitivity of embryonic tissues to transplacental carcinogenic action [10, 11, 14, 15]. The present writers have shown that an essential role in the realization of transplacental carcinogenic influences on embryonic mouse lungs of the sensitive line A is played not only by epithelial target cells, but also by mesenchymal cells and interaction between these tissue components [6-8]. The same factors are important for survival, growth, and differentiation of tissue explanted into culture [12]. An essential factor for normal organogenesis of the lungs is direct contact of the epithelial anlage with the mesenchyme, with a definite ratio between the numbers of cells of these tissue components; the limiting factor, moreover, is the presence of a "critical mass" of mesenchyme [3].

On the basis of the facts given above we postulate that local factors such as proliferative activity and the numerical ratio between epithelial and mesenchymal cells, and also the character of interaction between the tissue components in ontogeny may also play an important role in the realization of sensitivity of mice of a particular line to the development of lung tumors. It was accordingly decided to investigate these characteristics of lung tissue in mice of lines A and C57BL under normal conditions and during induced carcinogenesis. This paper gives the results of a comparative study of the relative numbers of epithelial and mesenchymal cells in organ cultures of embryonic lungs from mice of these lines.

EXPERIMENTAL METHOD

Minced lungs of 17-day A and C57BL mouse embryos, transplanted on to the surface of membrane filters (of the AUFS type, pore diameter 0.6 μ), resting on tantalum gauze platforms, placed in deep watch glasses, were used for culture. Into each watch glass was poured 1.5-2.0 ml of nutrient medium of the following composition: 71.5 ml of medium 199, 25 ml of bovine serum, 2.5 ml of concentrated extract of 11-day chick embryos, 1 ml of 40% glucose solution, per 100 ml of mixture. The material was cultured at 37°C in a constant gas mixture of atmospheric air and 5% CO_2; the nutrient medium was changed every 3-4 days. The explants were studied after 3 and 15 days of culture. ^{3}H-thymidine was added to the cultures on the

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