

jection of androgen during the first days of life modifies the sensitivity of enzyme systems and tissues to external factors, it can also be postulated that a single injection of testosterone propionate in the critical period of sexual differentiation of the hypothalamus enhanced the reactivity of the pararenal and intestinal tissue to DMH.

Neonatal androgenization caused thyroid pathology in 74% of male CBA mice. No precise explanation of this phenomenon can be given, but it can be tentatively suggested that a single injection of testosterone propionate into day-old animals can cause a breakdown of hypothalamic regulation of thyroid function in male CBA mice.

Neonatal androgenization thus has a modifying action on the development of DMH-induced pararenal angiosarcomas and intestinal tumors in male CBA mice.

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HUMAN TUMOR STRAINS TRANSPLANTABLE INTO NUDE MICE AND RATS

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This paper described the use of strains of carcinoma of the lung (CL-3) and of the larynx (CLar), Ewing's sarcoma (ES), fibrosarcoma (FS), Wilms' tumor (WI), and carcinoma of the kidney (CK) for transplantation into nude mice and rats. The above-mentioned strains are part of a collection of transplantable human tumors at the All-Union Oncologic Scientific Center, Academy of Medical Sciences of the USSR.

EXPERIMENTAL METHOD

Nude mice aged 6-8 weeks and nude rats aged 4-6 weeks, reared at the Institute, were used for transplantation. Strains CL-3, CLar, WT, and CK were obtained from material taken at operations. The tumor was transplanted in fragments into the mice. Strains ES and FS were obtained by transplantation of human tumor cell lines from tissue culture [4]. In that case 10^6 cells in 0.5 ml of medium were injected subcutaneously into mice. A suspension of human tumors after serial passages through mice was injected into the rats. The suspension contained 150 mg tissue in 0.5 ml. Subsequent serial transplantations in both rats and mice were carried out with tumor suspension.

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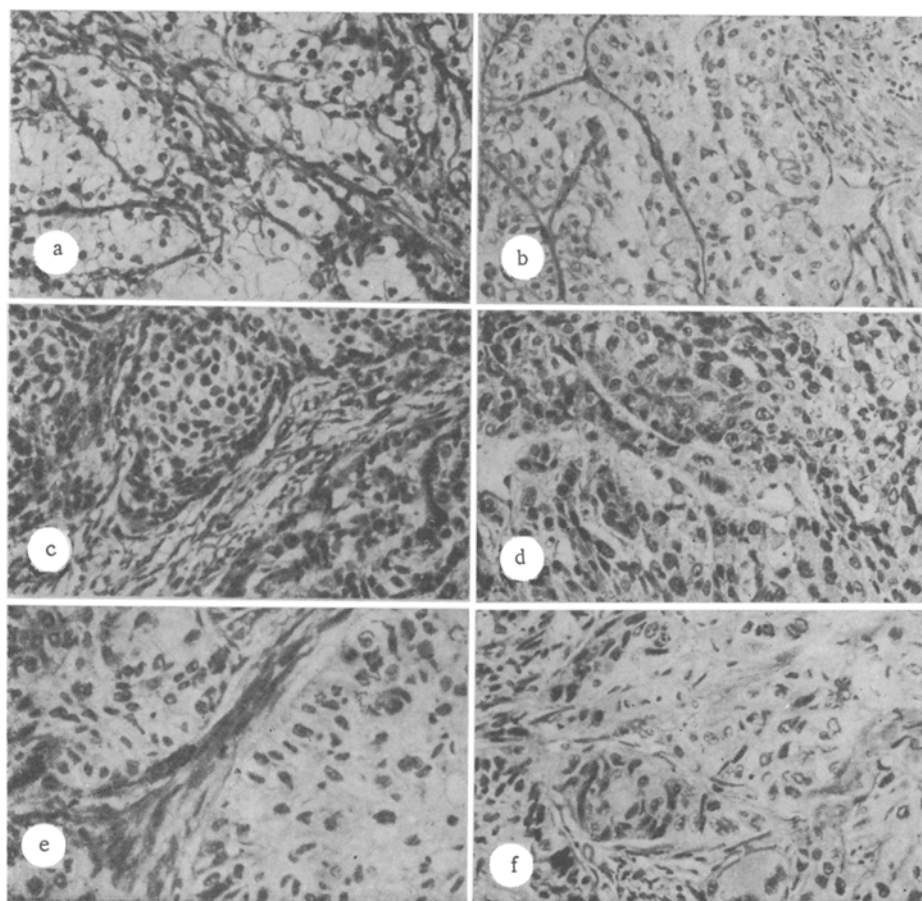


Fig. 1. Microscopic preparations of human tumors and strains obtained from them. a) Original tumor for strain CK (a pale-cell carcinoma of the kidney); b) strain CK at the 41st generation (pale-cell carcinoma); c) original tumor for strain WT (Wilms' tumor); d) strain WT, 41st generation; e) original tumor for strain CL-3 (squamous-cell carcinoma); f) strain CL-3, 9th generation (squamous-cell carcinoma of lung with tendency toward keratinization). a, c-f) Stained with hematoxylin and eosin, b) PAS reaction. 160 \times .

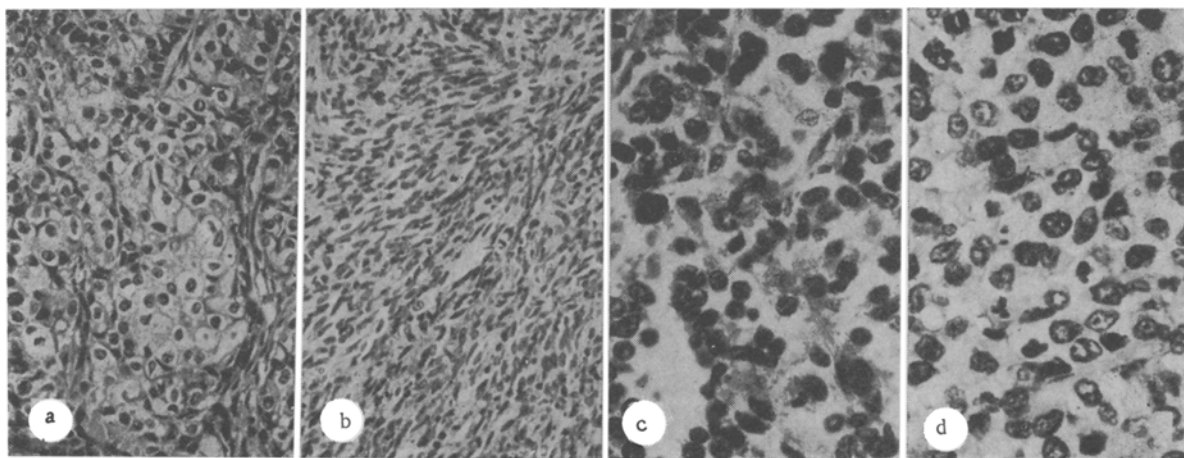


Fig. 2. Microscopic preparations of human tumors and strains obtained from them. a) Strain CLar, 29th generation (squamous-cell carcinoma with parakeratosis), hematoxylin-eosin, 160 \times ; b) strain FS, 1st generation (fibrosarcoma); hematoxylin-eosin, 160 \times ; c) original tumor for cell line ES (Ewing's sarcoma); hematoxylin-eosin, 400 \times ; d) strain ES, 40th generation, hematoxylin and eosin. a, b) 160 \times , c, d) 400 \times .

The histological characteristics of the tumors were studied in sections stained with hematoxylin and eosin, picrofuchsin, and the PAS reaction.

To determine the species specificity of tumors grown in nude animals, electrophoresis of lactate dehydrogenase in agar gel was used.

EXPERIMENTAL RESULTS

Strain CK was transplanted from animal to animal after 42-45 days. The original tumor in man had the structure of a pale-cell trabeculo-papillary carcinoma of the kidney (Fig. 1a). In the course of 42 generations the tumor preserved the basic structure of a pale-cell carcinoma (Fig. 1b), acquiring the structure of a papillary adenocarcinoma in individual generations.

Strain WT was transplanted after 22-24 days. Throughout 57 generations it preserved the structure of a nephroblastoma with some predominance of the epithelial component over cells forming bands, solid structures, and something resembling tubules. Mesenchymal components were less well represented in the tumor. Rosette-like and pseudotubular structures were present. In all passages the strain corresponded in structure and cell composition basically to the original tumor (Fig. 1c, d). Strain CL-3 was transplanted after an interval of 30-32 days. During passage it preserved a basically typical structure corresponding to the pattern of squamous-cell carcinoma with signs of parakeratosis and a more or less well marked tendency toward keratinization (Fig. 1e, f).

Strain CLar was transplanted after an interval of 14-16 days. Throughout 40 passages this strain corresponded to the original tumor in man and preserved the structure of a squamous-cell carcinoma with no signs of keratinization (Fig. 2a).

The source for strain FS was a line of tumor cells obtained in 1976, and subsequently undergoing many passages in tissue culture before transplantation into animals. This strain was transplanted from animal to animal after 15-18 days. In all generations it preserved the stereotyped structure of a fibrosarcoma with collagen production (Fig. 2b).

Strain ES, although the tumor cells had gone through 50 passages in tissue culture before transplantation, still preserved the structure of the original tumor from which the cell line was obtained (Fig. 2c). The strain was transplanted into animals after 13-15 days, and by now has undergone 72 passages. During passage the strain preserved its standard structure and the cell composition of Ewing's sarcoma. The cells were circular with vesicular nuclei and delicate chromatin (Fig. 2d). In some passages the formation of pseudorosettes was observed, alternating with a more solid arrangement of the cells. Impregnation with silver revealed the virtual absence of an argyrophilic skeleton in the tumor. Treatment with Schiff's reagent revealed a large quantity of glycogen in the cytoplasm of individual cells and intercellular spaces.

All seven strains transplanted into nude mice and rats consisted basically of human cells. This is shown by the five peaks of the enzyme lactate dehydrogenase, revealed on electrophoresis.

The strains of human tumors transplanted into nude mice and rats constitute a convenient experimental model for molecular biological research into human tumors; for example, to detect oncogenes and their expression in human tumor cells, and also to find oncoproteins [1-3]. The availability of these models means that the experimenter can be constantly supplied with the necessary quantity of tumor mass, with stable properties characteristic of transplantable tumor strains.

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