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16 October 1969

ST-Feline Fibrosarcoma Virus: Induction of Tumors in Marmoset Monkeys

Abstract. *Two newborn marmosets, inoculated with a cell-free extract of feline fibrosarcomas, developed multiple sarcomas and died within 46 days of inoculation, whereas two of these animals inoculated with a crude homogenate developed no tumors. This susceptibility to a mammalian RNA sarcoma virus suggests that marmosets may be particularly suitable for attempts to isolate infectious agents from man.*

The cell-free transmission of a feline fibrosarcoma between kittens, and from kittens to newborn dogs and rabbits, was described by Snyder and Theilen (*1*). We describe here the inoculation of marmoset monkeys (*Saguinus fuscicollis*) with tumor homogenates and cell-free extracts of feline fibrosarcomas and their subsequent development of multiple sarcomas.

A tumor homogenate was prepared from a pool of four experimentally induced feline fibrosarcomas (*2*). A crude 25 percent tumor suspension was prepared in tris-ethylenediaminetetraacetate buffer at *p*H 7.0, homogenized in a mortar with sterile sand, and centrifuged at 600*g* for 15 minutes. The supernatant was inoculated intraperitoneally (0.25 ml) and subcutaneously (0.25 ml) into both a newborn and a 3-day-old marmoset. One animal died with bacterial enteritis at 4 weeks after inoculation without signs of tumor development; the other animal is alive and normal 14 weeks afterward.

A cell-free extract was prepared from the same pool of feline fibrosarcomas by Moloney's technique (*3*). The extract, in 0.5 g tumor equivalents per animal, was inoculated intraperitoneally and subcutaneously in divided doses into a newborn and into a 3-day-old marmoset. Both animals developed palpable masses in the right inguinal area by 3½ to 4 weeks after inoculation. They died 4 weeks and 46 days, respectively, after inoculation, and in both animals inguinal and multiple intraabdominal tumors were found. The largest tumor, 3.0 cm in diameter, was found in the animal that died 46 days after inoculation. It was located on the left side of the abdomen, contralateral to the intraperitoneal inoculation site and extended from the stomach anteriorly to the kidney posteriorly. In both animals lesions were absent at the sites of subcutaneous inoculation.

Tumor tissues were collected at necropsy for light and electron microscopy and for in vitro culture. The densely cellular tumors were classified as fibrosarcomas (Fig. 1), although they were composed of two cell types, fusiform and polygonal. Mitoses were numerous in both cell types. Fusiform cells with variable amounts of intercellular collagen comprised 80 to 90 percent of the tumor masses in the animal with the longer course, and in this animal neoplastic tissue had invaded stomach, urinary bladder, and skeletal muscle surrounding the inguinal mass. In the other animal, polygonal-shaped mononuclear cells predominated in the tumors and diffuse mesothelial cell hyperplasia was seen along visceral and parietal peritoneal surfaces. These hyperplastic mesothelial cells were identical histologically to the polygonal-shaped tumor cells. Hemorrhage and necrosis were present in some tumors, but no inflammatory cells were detected within the tumor masses. Electron microscopic study of 100 tumor cells from the animal with the shorter course revealed no viral particles. Tumor cells from both animals are growing in in vitro cell culture and are currently in the 6th and 14th serial cell passages, respectively. They have a modal chromosome number of 46, the normal diploid number for marmosets, and the karyotype is essentially normal. Although a mixture of large mononuclear and fibroblastic cells is still present in the cell cultures, the proportion of fibroblastic cells has increased.

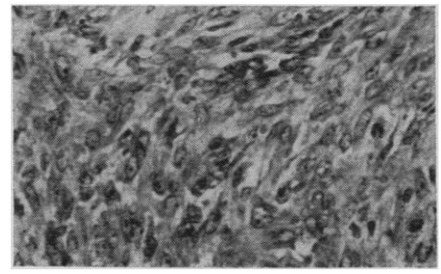

Fig. 1. Photomicrograph of an abdominal tumor from a marmoset that died 46 days after inoculation with ST-feline fibrosarcoma virus (hematoxylin and eosin stain; × 220).

In addition to the susceptibility of marmosets to a mammalian RNA sarcoma virus reported here, it was shown previously that marmosets are more susceptible to certain avian sarcoma viruses (*4–6*) than other nonhuman primates (*7, 8*). The reason for this is unknown, but, even before we understand the reason, marmosets seem to be a prime choice as experimental animals in attempts to isolate similar agents from human malignancies.

Note added in proof: Since this report was submitted, tumors have been induced in four more marmosets, and C-type virus particles have been demonstrated in cultured tumor cells by electron microscopy.

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9. Supported by contract PH 43-62-179, Special Virus Cancer Program, National Cancer Institute.

3 November 1969