Induction of Tumors in Hamsters with an Avian Adenovirus (CELO)

Abstract. *When newborn hamsters were inoculated subcutaneously with chicken-embryo lethal orphan virus, tumors developed at the site of inoculation in 23 out of 69 hamsters within 88 to 195 days of inoculation. These tumors and tissue cultures, prepared from a primary tumor, were transplantable to newborn and weanling hamsters. The primary tumors and tissue cultures of a primary tumor were free of demonstrable infectious virus. The virus is the first "nonhuman" adenovirus found to induce tumors in hamsters.*

The chicken-embryo lethal orphan (CELO) virus was first isolated and described by Yates and Fry (*1*) as an endogenous virus of chicken eggs. The virus has since been isolated as a contaminant of chicken embryos or chicken-embryo tissue cultures (*2*). A recent report of virus isolation from chicken trachea (*3*) and the report of widespread occurrence of antibody to this virus in chicken flocks (*1, 4*) indicate that the virus may be responsible for inapparent or mild infection of the respiratory tract of chickens.

Our interest in this virus was aroused when it was reported that the virus had the morphological structure and many of the properties of adenovirus (*5*). We now report on its oncogenic potential in newborn hamsters.

Two litters of Golden Syrian hamsters (No. 1, eight animals; and No. 2, four animals) were inoculated subcutaneously on the day of birth with a high-titer virus (0.1 ml to each animal) (*6*). The animals were examined regularly, and 147 days later, one hamster of litter No. 2 was found with a subcutaneous tumor, 20 mm in diameter, at the site of inoculation.

On the 152nd day, this tumor, now 45 mm, was surgically removed, minced, and transplanted into groups of newborn and weanling hamsters. The tumor was extremely hard in consistency and had the histological appearance of a well-differentiated fibrosarcoma with a small amount of collagen production (*7*).

On the 195th day, two additional hamsters (litter No. 2) had 10-mm tumors at the site of inoculation. On the 236th day, one of the tumors, measuring 45 mm, was surgically removed. This tumor was also hard in consistency and was histologically identical to the previous tumor studied. It was minced into fine pieces and produced tumors when transplanted into newborn and weanling hamsters (Table 1).

Monolayer tissue cultures prepared from this tumor have the characteristics of "transformed" cells, such as pleomorphic cell morphology, rapid and disorganized cell growth, and increased glycolysis. Inoculation of the cultured cells (10,000 cells or more per site) into newborn and weanling hamsters has resulted in the development of tumors in the inoculated animals (Table 1).

Serum samples collected at biweekly intervals from tumor-bearing hamsters have as yet given no significant reactions in complement-fixation tests with homologous tumor antigens. These serums did not react with 1:2 dilutions of normal chicken-embryo fibroblast-cell antigens, normal hamster-cell antigens, or with antigens characteristic of hamster tumors induced by Schmidt-Ruppin Rous sarcoma, SV40, and polyoma viruses, or by adenovirus, types 7, 12, and 18 (*8, 9*).

Clarified extracts (20 percent) of the primary and transplanted CELO hamster tumors failed to react in complement-fixation tests with hamster serums containing the avian leucosis and sarcoma group-specific complement-fixing antibodies (*8*), thus ruling out the possibility that the hamster tumors induced with CELO virus were due to an avian sarcoma contaminant of the virus inoculum (*10*). The CELO hamster tumor antigens also failed to react with serums from hamsters with tumors induced by adenovirus types 7, 12, and 18; tumors induced by SV40 and polyoma viruses were also negative.

Even after intensive search, we failed to find infectious CELO virus in primary hamster tumors and in tissue-culture cells grown from a primary tumor. Other stocks of CELO virus also induced tumors in hamsters (Table 1).

The CELO virus is the first nonhuman adenovirus found to induce tumors in hamsters. To date we have failed to induce tumors in newborn hamsters with GAL (Gallus, adenolike) virus, an avian adenovirus (*11*).

Table 1. Development in hamsters of primary and transplanted CELO-virus–induced tumors.

Expt. No.	Inoculum	Hamsters developing tumors		Time to 1st 10-mm tumor (days)	Tumor size	
		NB* (No.)	Weanling (No.)		Time (days)	Size (mm)
1	CELO virus	3/12†		147–195	236	30–45
2	CELO virus	1/15		90	111	35
3	CELO virus	9/22		98–111	182	25–70
4	CELO virus	10/20		88–126	126	10–35
5	Primary tumor No. 6, minced from Expt. 1	3/16	7/14	20–54	54	10–60
6	TC*-grown No. 6 (2nd TC Pass.)	15/15	6/10	19–36	36	10–40

* NB, newborn (less than 24 hours); TC, tissue culture. † Numerator indicates number with tumors; denominator indicates number inoculated.

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References and Notes

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