Comparative Susceptibility of Non-inbred and Strain LSH Inbred Syrian Hamsters to the Oncogenic Adenoviruses[1] (34805)

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Noninbred Syrian hamsters (*Mesocricetus auratus*) are commonly used in experimental viral oncology and readily accept tumor allografts although isoantigenic disparity may complicate the interpretation of results in studies on tumor immunity in which attempts are made to demonstrate antigenic differences between normal and tumor cells.

Strain LSH was obtained and foster nursed on noninbred hamsters to eliminate enzootic viruses (1, 2). Inbred strains of animals have been observed to vary in their susceptibility to various microbial agents and strains of mice resistant to the oncogenic effects of polyoma virus and adenovirus type 12 (A-12) have been reported (3, 4). Therefore, the comparative susceptibility of noninbred and LSH inbred hamsters to A-12 and the simian adenovirus SA-7 were studied prior to utilization of the LSH animals instead of noninbred animals for testing the oncogenic effects of various viruses and studies to demonstrate tumor-specific antigens.

Materials and Methods. Viruses. Human adenovirus type 12 (A-12), strain Huie, used in these experiments was a plaque-purified, adeno-associated virus (AAV)-free strain (5) obtained from Dr. Bruce Casto, Chicago, Illinois. The virus was propagated in our laboratory in either primary human embryonic kidney (HEK) cells or HEP-II cells. The titer of the virus used in these experiments was $10^{7.0}$ $TCID_{50}$ per 1.0 ml in HEK cells. Simian adenovirus (SA-7) was also obtained from Dr. Casto and subsequently propagated in our laboratory in a continuous line of green monkey kidney cells, designated as BSC-1. The infectivity titer of the virus used in these experiments was $10^{8.5}$ $TCID_{50}$ per 1.0 ml in BSC-1 cells.

Animals. Animal care procedures and housing have been previously described (1). Hamsters less than 24 hr of age were inoculated with 0.1 ml by the subcutaneous (sc) or intraperitoneal (ip) route. Inoculated animals were weaned and separated by sex at 21–28 days and observed for tumor formation. Only animals coming to adequate necropsy are included in the tabulations. Necropsies were performed on all animals that were found dead or that were sacrificed when moribund by exsanguination or euthanasia.

Results. The incidence of A-12 and SA-7 tumors in noninbred and strain LSH hamsters is shown in Table I. The noninbred animals are significantly more susceptible to the oncogenic effects of A-12 than the LSH strain ($p = .01$). The 94% incidence of SA-7 tumors in the LSH strain is not significantly higher than the 91% incidence observed in the noninbred animals. Although there are still a few animals alive, it appears improbable that many, if any, will develop tumors because of the long observation period to date.

Since females have been reported to be more susceptible than males to tumor induction with A-12 (6), and since the ip route is more sensitive with low doses of virus (7), the A-12 data have been further analyzed and these variables separated (Table II). Data

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TABLE I. Incidence of A-12 and SA-7 Tumors in Noninbred and Strain LSH Hamsters.

Virus	Animals	Percentage with tumor	Mean age (days) at death		Number weaned	Number alive (mean days alive)
			With tumor	Without tumor		
A-12	Noninbred	90 (26/29)[a]	61	—	33	3 (470)
	LSH inbred	48 (15/31)	51	184	33	7 (450)
SA-7	Noninbred	91 (21/23)	43	55	25	1 (453)
	LSH inbred	94 (32/34)	49	45	34	0 —

[a] Number with tumor over total of number necropsied and number alive.

TABLE II. Analysis by Sex of A-12 Tumor Incidence in Noninbred and Strain LSH Hamsters.

Sex	Animals	Route	Percentage with tumor	Mean tumor latent period	Number alive
Males	Noninbred	ip	100 (11/11)[a]	52	0
	LSH inbred	ip	46 (5/11)	60	1
Females	Noninbred	ip	100 (10/10)	59	0
	LSH inbred	ip	55 (6/11)	45	2

[a] Number with tumor over total of number necropsied and number alive.

for the sc route is not included because of the small number of animals involved.

When males inoculated by the ip route are compared, noninbred males are significantly more susceptible than inbred males, *i.e.*, 100% with tumors as compared with 46% with tumors ($p = <.005$). The same conclusion can be drawn from comparing the noninbred females inoculated by the ip route with comparable LSH females ($p = <.025>.01$). There is no apparent significant sex difference in tumor incidence within either of the groups in this study; although the number of animals per group is not large, they do include hamsters from different litters with each inoculum.

Discussion. Resistance and susceptibility should be considered as relative terms. There are numerous examples in which relative resistance can be overcome by overwhelming doses of a particular agent or with microorganisms of a highly virulent strain. The strain of adenovirus-12 used in these studies may be regarded as more oncogenic than other strains employed in the past (8) as 100% of noninbred hamsters of both sexes developed tumors with a mean tumor latent period of less than 60 days. Although AAV, *per se,* has been reported not to interfere with tumor induction (9), it does interfere with the growth of virus *in vitro* (10). Therefore, since the oncogenic effects of A-12 are dose-dependent, the presence of AAV may indirectly affect the oncogenicity by contributing to diminished titers of virus pools. It thus appears that the strain of A-12 employed in these studies was highly oncogenic in part because of the absence of AAV. The enhanced oncogenicity provides at least one possible explanation for the absence of a sex difference in the incidence of tumors with either strain of hamsters.

Similarly, the shorter mean tumor latent periods with SA-7 (cf Table I) in noninbred hamsters suggest that it is more highly oncogenic than A-12. Therefore, potential differences in susceptibility between the strains are not manifest with the highly oncogenic SA-7 just as differences between sexes were not manifest with the strain of A-12 employed in these studies. It appears probable that differences in susceptibility between the noninbred and LSH inbred hamsters would be of greater magnitude with the weakly

oncogenic adenoviruses such as human types 3, 7, 14, and 21.

Summary. The comparative susceptibility of noninbred Syrian hamsters (*Mesocricetus auratus*) and the LSH strain of inbred hamsters to the oncogenic effects of adenoviruses type 12 and SA-7 has been studied. Noninbred animals are significantly more susceptible to adenovirus type 12. However, with SA-7 the incidence of tumors in noninbred hamsters was slightly but not significantly lower than in LSH hamsters.

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