

# QUANTITATIVE ANALYSIS OF THE IMMUNOGENIC ACTIVITY OF SV40 VIRUS AND OF TUMOR CELLS INDUCED BY THIS VIRUS

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A study of specific antitumor immunity created in Syrian hamsters by oncogenic virus SV40 and by tumor cells induced by the same virus showed that the level of specific resistance depends on the immunizing dose of virus and cells. Investigation of the resistance-inducing activity of a wild strain of SV40 virus showed that the minimal dose inducing resistance in hamsters was ten times higher than for the tsA-30 mutant of the virus. The minimal resistance-inducing dose of irradiated cells of a tumor induced by the same strain of SV40 virus was  $9 \cdot 10^5$  cells; a tenfold increase in the dose led to a significant increase in the level of specific antitumor immunity. KEY WORDS: SV40 virus; tumors; immunity.

The immunogenicity of tumors is determined by the presence of a specific transplantation tumor antigen (STTA) on the tumor cell membrane. Attempts to measure the protective properties of tumors of varied etiology quantitatively have been undertaken by several workers [4-6, 8]. Virus carcinogenesis has provided a model with which to study the various aspects of the mechanism of STTA synthesis, including the quantitative principles of its induction in vivo and in vitro.

In the present investigation the level of specific antitumor immunity induced in Syrian hamsters by various doses of wild-type SV40 virus, its thermosensitive A-mutant, and cells of a tumor induced by SV40 virus was determined.

## EXPERIMENTAL METHOD AND RESULTS

It was shown previously that some strains of tsA-mutants of SV40 virus are defective in their ability to induce synthesis of STTA in hamsters in vivo and in vitro. In the present investigation attempts were made to determine the resistance-inducing dose of SV40 virus (wild strain and tsA mutant) and of the cells of a tumor induced in a Syrian hamster by the wild strain of SV40 virus. For immunization with strains of SV40 virus, tenfold concentrations of the wild strain of the virus, its tsA-30 mutant, and their tenfold dilutions were used. Resistance-inducing activity of each dose of virus was determined two weeks after a single intraperitoneal immunization in the transplantation test in hamsters using Murka's modification [2]. The results are given in Table 1. They show that the minimal immunizing dose for the wild strain of SV40 virus corresponded to  $10^{6.3}$  tissue cytopathogenic doses (TCD<sub>50</sub>) in 1 ml, in agreement with results obtained by other workers [1, 3]. A tenfold increase in the immunizing dose of the wild strain of SV40 virus led to a proportionate increase in the level of specific antitumor immunity in the hamsters. Increasing the dose by 100 times led to a further rise in the level of immunity. The minimal resistance-inducing dose of strain tsA-30 was found to be  $10^{8.5}$  TCD/ml.

The results showing resistance-inducing activity of irradiated cells of a tumor induced by SV40 virus are given in Table 2. They show that on immunization of hamsters with tumor cells the minimal immunizing dose was  $9 \cdot 10^5$  cells per hamster. An increase in the minimal immunizing dose of tumor cells by about 10 times increased the level of immunity to the tumor by about 100 times. The level of specific resistance thus depended directly on the immunizing dose of SV40 virus and of tumor cells induced by this virus. Significant quantitative differences also were demonstrated in the resistance-inducing activity of the wild strain SV40 and its tsA-30 mutant. It was found previously that hamster cells transformed by the tsA-30 mutant of SV40 virus are virtually free from STTA (the immunogenic dose of these cells in vivo was more than 100 times greater than the immunogenic dose of cells transformed by the wild strain of SV40 virus).

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TABLE 1. Quantitative Differences in Resistance-Inducing Activity between Wild Strain of SV40 Virus and Its tsA-30 Mutant

Immunizing material		Results of transplantation test*		
strain of virus	infectious activity, log TCD <sub>50</sub>	lg PD <sub>50</sub> (±SE)	lg IR	t
Control (no virus injected)	—	0,50±0,31	—	—
Wild strain of SV40	8.3 7.3 6.3 5.3	>4,2±0,30 ≥1,9±0,35 ≥1,47±0,39 0,77±0,33	>3,70 ≥1,40 ≥0,97 0,27	>8,8 ≥2,9 ≥1,9 0,5
Mutant tsA-30	8.5 7.5 6.5	≥4,4±0,35 1,0±0,65 0,78±0,34	≥3,90 0,50 0,28	≥9,3 0,7 0,6

\* Log PD<sub>50</sub> indicates logarithm of dose of cells of test tumor which, when transplanted, gave tumor growth in 50% of animals; log IR denotes logarithm of index of resistance.

TABLE 2. Dependence of Level of Specific Resistance in Hamsters Immunized with Various Doses of Tumor Cells Induced by SV40 Virus

Immunizing material	No. of cells injected into hamster	Results of transplanta. test with tumor induced by SV40 virus †	
		log PD <sub>50</sub>	log IR
Control (no virus injected)	—	1,2	—
Cells of tumor induced by wild strain of SV40 virus (E-1)*	7.5·10 <sup>6</sup> 3.7·10 <sup>6</sup> 9.0·10 <sup>5</sup> 4.5·10 <sup>5</sup> 3.4·10 <sup>5</sup> 1.8·10 <sup>5</sup>	4.90 3.90 2.30 1.60 1.40 1.30	3.70 2.70 1.10 0.40 0.20 0.10

\* All samples of cells were irradiated in a dose of 12,000 rad before injection into hamsters.

† Legend as in Table 1.

To sum up the results it can thus be said that the resistance-inducing activity of SV40 virus in vitro correlates with STTA synthesis in cells transformed by the virus.

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