[16] Maas, W. K., in *Cold Spring Harbor Symposia on Quantitative Biology*, vol. 26, (1961), p. 183.
[17] Neidhardt, F. C., in "Régulations chez les microorganismes," *Colloq. Intern. Centre Natl. Rech. Sci. (Paris)*, **124**, 329 (1963).
[18] Nakada, D., and B. Magasanik, *Biochim. Biophys. Acta*, **61**, 835 (1962); *J. Mol. Biol.*, **8**, 105 (1964).
[19] Kepes, A., *Biochim. Biophys. Acta*, **76**, 293 (1963).
[20] Doi, R. H., and R. T. Igarashi, these PROCEEDINGS, **52**, 755 (1964).
[21] Chaloupka, J., and P. Kreckova, *Biochem. Biophys. Res. Commun.*, **8**, 120 (1962); *ibid.*, **12**, 380 (1963).
[22] Millet, J., and J. P. Aubert, *Compt. Rend.*, **259**, 2555 (1964).
[23] Spizizen, J., B. Reilly, and B. Dahl, in *Abstracts*, Eleventh International Congress on Genetics, The Hague, 1963.
[24] Bernlohr, R. W., *J. Biol. Chem.*, **239**, 538 (1964).
[25] Balassa, G., *Biochem. Biophys. Res. Commun.*, **15**, 236 and 240 (1964).
[26] Fitz-James, P. C., in "Régulations chez les Microorganismes," *Colloq. Intern. Centre Natl. Rech. Sci. (Paris)*, **124**, 529 (1963).
[27] Ryter, A., *Ann. Inst. Pasteur*, **108**, 40 (1965).
[28] Norris, R., bibliography in *J. Gen. Microbiol.*, **28**, 393 (1962).
[29] Baillie, A., and J. R. Norris, *J. Bacteriol.*, **87**, 1221 (1964).
[30] Greenberg, R. A., and H. O. Halvorson, *J. Bacteriol.*, **69**, 45 (1955).
[31] Powell, J. F., and R. E. Strange, *Biochem. J.*, **63**, 661 (1956).
[32] Strange, R. E., and F. A. Dark, *J. Gen. Microbiol.*, **17**, 525 (1957).
[33] Sebald, M., and P. Schaeffer, *Compt. Rend.*, **260**, 5398 (1965).
[34] Bernlohr, R. W., and G. D. Novelli, *Biochim. Biophys. Acta*, **41**, 541 (1960); *Arch. Biochem. Biophys.*, **103**, 94 (1963).
[35] Balassa, G., H. Ionesco, and P. Schaeffer, *Compt. Rend.*, **257**, 986 (1963).
[36] Aubert, J. P., J. Millet, E. Pineau, and G. Milhaud, *Biochim. Biophys. Acta*, **51**, 519 (1961).
[37] Powell, J. F., *Biochem. J.*, **54**, 210 (1953).
[38] Ryter, A., H. Ionesco, and P. Schaeffer, *Compt. Rend.*, **252**, 3675 (1961).
[39] Fitz-James, P., in *Abstracts*, Eighth International Congress on Microbiology, Montreal, 1962 p. 16.
[40] Spizizen, J., these PROCEEDINGS, **44**, 1072 (1958).
[41] Thorne, C. B., *J. Bacteriol.*, **83**, 106 (1962).
[42] Takahashi, I., *J. Bacteriol.*, **89**, 294 (1965).
[43] Jacob, F., and J. Monod, *J. Mol. Biol.*, **3**, 318 (1961).
[44] Stanier, R. Y., *Bacteriol. Rev.*, **14**, 179 (1950).

---

*STUDIES OF ADENOVIRUS-SV40 HYBRID VIRUSES, III. TRANSFER OF SV40 GENE BETWEEN ADENOVIRUS TYPES**†

BY WALLACE P. ROWE

LABORATORY OF INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, BETHESDA, MARYLAND

Communicated by R. J. Huebner, July 30, 1965

A number of adenovirus types have become "hybridized" with at least a portion of the SV40 viral genome as a consequence of prolonged passage in monkey kidney cultures contaminated with SV40 virus.[1-5] The adenovirus 7 (Ad. 7)-SV40 hybrid strain E46+ has been shown to consist of a mixture of nonhybrid adenovirus particles which are fully infectious for human embryonic kidney (HEK) cells in tissue culture but markedly limited in ability to propagate in African green monkey kidney (AGMK) cell cultures, and hybrid particles which are defective (i.e., single

particles cannot initiate replicative infection) in both HEK and AGMK cells.[6-8] Production of new hybrid particles in either HEK or AGMK cells occurs only in cells dually infected with a hybrid and a nonhybrid particle, and production of nonhybrid virus in AGMK cells is similarly dependent on dual infection. The SV40 genetic material apparently codes for formation of a protein which facilitates adenovirus growth in monkey cells but which is not required in human cells.[9, 10]

Because of the interaction between adenovirus particles in E46+, experiments were carried out to determine if dual infection by E46+ and other adenovirus types would result in transfer of the SV40 gene to the previously nonhybrid adenovirus.

Materials and Methods.—Viruses: The E46+ strain of Ad. 7-SV40 hybrid virus was grown in AGMK cultures, being used in the present experiments at the 7th and 8th AGMK passage level after pool E46.[1, 6] E46−, the nonhybrid adenovirus recovered from E46, was grown in HEK cultures. Other adenovirus strains used were the prototype strains,[11] grown in KB or HEK cells; none of these strains induced SV40 neoantigen (T antigen) in HEK cells, and with the exception of Ad. 12, none had ever been passed in monkey cells. Titrations were carried out by the plaque procedure in HEK cells.[7] Adenovirus antisera were prepared by hyperimmunization of rabbits with crude tissue culture grown virus preparations.[12]

Cultures: Dual infection experiments were done in tube cultures of primary AGMK cells. The cultures were held in a stationary position at 36°C, and were maintained in medium consisting of Eagle's basal medium (BME) with 2% inactivated agammaglobulinic calf serum, penicillin, streptomycin, and glutamine.

SV40 neoantigen assay: Ability of adenovirus preparations to induced SV40 neoantigen was determined by the immunofluorescent procedure, using techniques described previously.[6, 13] Petri dish cultures of HEK cells growing on coverslips were inoculated with 0.1 ml of undiluted or a 10^{-1} dilution of test material, and 24 hr later the coverslips were fixed in cold acetone, dried, treated with SV40-tumored hamster serum, and stained with fluorescein-conjugated goat anti-hamster globulin. The percentage of cells showing the characteristic nuclear fluorescence was then determined. In some experiments the percentage of cells stained with Ad. 12-tumored hamster serum was also determined; the ratio of percentage staining with Ad. 12 serum to that with SV40 serum (the Ad/SV40 staining ratio) was taken as a measure of the relative amounts of adenovirus and SV40 genetic material in the virus population.[6]

Results.—Transfer of SV40 gene from E46+ to various adenoviruses: Initial experiments consisted of infecting AGMK tube cultures with mixtures of prototype nonhybrid adenovirus strains with E46+, and carrying the progeny by undiluted virus passage in AGMK cultures; at various passage levels, sublines were initiated with Ad. 7 rabbit antiserum to reduce or eliminate the "donor" virus. The antiserum-treated passage lines were tested for hybrid virus of the recipient serotype by inoculating HEK coverslip preparations with mixtures of the harvests and various rabbit antisera, and 24 hr later fixing and staining for SV40 neoantigen (Table 1). At all passage levels the preparations induced SV40 neoantigen, and the antigen induction was prevented by treating the inoculum with rabbit antiserum to the recipient serotype, but not with Ad. 7 antiserum. The Ad. 2 passage line, freed of Ad. 7 virus by antiserum treatment and AGMK limiting dilution passage, also induced SV40 neoantigen (pool 1017, Table 1), further indicating that residual Ad. 7 virus was not responsible for the SV40 neoantigen induction.

In these experiments, the nonhybrid adenoviruses inoculated into AGMK cultures without E46+ could not be maintained in serial passage, but the progeny of the mixed infections passed without difficulty in the presence of Ad. 7 antiserum.

In a similar experiment in which $10^{5.1}$ pfu of Ad. 15 were inoculated into AGMK cultures with $10^{6.4}$ pfu of E46+, and the harvest was passed with Ad. 7 antiserum,

TABLE 1

ESTABLISHMENT OF ADENOVIRUS-SV40 HYBRID VIRUSES BY MIXED INFECTION WITH E46+ FOLLOWED BY PASSAGE WITH AD. 7 ANTISERUM

Expt. no.	Virus Grown with E46+ Type	Virus Grown with E46+ Pfu/tube*	Passages in AGMK: Passages without antiserum	Passages in AGMK: Subsequent passages with Ad. 7 RS	Dilution assayed	Assay of Harvest for SV40 Neoantigen Induction (per cent of cells stained): Harvest + normal RS†	Harvest + Ad. 7 RS	Harvest + Ad. 2 RS	Harvest + Ad. 2 RS and helper virus‡	Harvest + Ad. 4 RS	Harvest + Ad. 5 RS	Harvest + Ad. 12 RS	Harvest + SV40 RS
1	Ad. 2	8.3	1	1	10^0	9.0	...	0	...	...	...	...	..
			2	1	"	4.6	...	0	...	...	...	...	..
			5	2	$10^{-0.5}$	1.6	2.6	0	...	...	...	...	..
			5	3	"	3.2	6.2	0	...	...	...	...	..
			5	3§	10^0	50	30	0.002	0.01	...	...	...	40
2	Ad. 2	8.0	1	1	10^0	2.6	1.7	0	...	...	...	...	..
3	Ad. 4	5.3	1	1	10^0	30	20	...	...	0.02	...	...	..
4	Ad. 5	5.7	1	1	10^0	5.2	5.2	...	...	...	0.01	...	..
5	Ad. 12	5.2	1	1	10^0	30	35	...	...	...	...	0.004	..
6	Ad. 12	5.2	1	1	10^0	1.9	0.8	...	...	...	...	0	..

* Log_{10} of the number of plaque-forming units inoculated per AGMK culture. Each virus was mixed with $10^{6.4}$ or $10^{6.5}$ pfu of E46+.
† RS = rabbit serum. All rabbit sera were used at 1:20 dilution.
‡ $10^{6.2}$ pfu of E46− were added to the assay cultures.
§ Pool 1017, further freed of Ad. 7 by limiting dilution passage in AGMK.

TABLE 2

HYBRIDIZED DONOR AND RECIPIENT VIRUSES IN HARVESTS OF MIXED INFECTION OF AGMK CELLS

Expt. no.	"Donor Virus" Type	"Donor Virus" Pfu/tube*	Nonhybrid Recipient Virus Type	Nonhybrid Recipient Virus Pfu/tube	Infectivity titer in HEK $TCID_{50}$/0.1 ml (log_{10})	Assay of Harvest of Mixed Infection: SV40 neoantigen induction (per cent of cells stained)†: Harvest + normal RS	Harvest + Ad. 7 RS	Harvest + Ad. 2 RS	Harvest + Ad. 7 and Ad. 2 RS	Harvest + SV40 RS
1	E46+	6.4	Ad. 2	8.3	...	17.7	9.2	8.4	0.25	..
	"	"	None	—	...	95	0.02	85	...	..
2	E46+	6.5	Ad. 2	8.0	7.2‡	65	15	40	0.03	..
	"	5.5	"	"	7.2‡	50	35	2.5	0.02	..
	"	6.5	None	—	...	95	0.01	...	...	..
	None	—	Ad. 2	8.0	4.2	0	...	...	...	..
	SV40	7.0	"	"	>7.5§	...	...	...	...	0
	SV40 preinfected		"	"	>7.5§	...	...	...	...	0
	SV40	7.0	None	...	...	0	...	...	...	..
3	E46+	6.5	Ad. 2	8.0	...	65	12	19	0.02	..
	E46+ + E46−RS		"	"	...	0.006	0	0	0	..
4	Ad. 2+ (pool 1017)	7.0	E46−	7.3	...	66	35.3	34.7	0.25	..

* Log_{10} of the number of plaque-forming units inoculated per culture tube.
† The harvests were assayed by inoculation of 0.1 ml of undiluted virus mixed with 0.1 ml of 1:20 dilution of rabbit serum (RS).
‡ Titration done in cultures maintained in medium containing 0.5% Ad. 7 rabbit antiserum. The virus at the end point dilution was identified as Ad. 2.
§ Titration done in cultures maintained in medium containing 0.5% SV40 rabbit antiserum.

only minimal, late cytopathogenicity developed, indicating that little or no transfer of the SV40 gene had occurred.

These results clearly showed that adenovirus types 2, 4, 5, and 12 acquired SV40 genetic material from E46$^+$ virus within a single passage of the virus mixture; however, this procedure did not permit an estimate of the amount of hybridized recipient virus. To answer this question, the following type of experiment was performed. AGMK cultures were inoculated with mixtures of Ad. 2 and E46$^+$; 4 hr later the tubes were rinsed 4 times with 2 ml of BME, and maintenance medium was added. The harvests, obtained when CPE were complete, were assayed in HEK coverslip dishes in the presence of (1) normal rabbit serum (to estimate the total amount of hybrid virus); (2) Ad. 7 rabbit antiserum (to estimate the amount of hybridized Ad. 2); (3) Ad. 2 rabbit antiserum (to estimate the amount of E46$^+$); and (4) a mixture of Ad. 7 and Ad. 2 rabbit antisera (to verify the potency of the antisera). The coverslips were fixed at 24 hr and stained with SV40-tumored hamster serum. The results, shown in Table 2, indicate that the amount of hybridized Ad. 2 (Ad. 2$^+$) produced by the mixed infection was generally equivalent to the yield of hybrid Ad. 7. When a lower multiplicity of E46$^+$ was used, the yield of Ad. 2$^+$ was about 10 times that of E46$^+$ (Table 2, expt. 2, line 2).

Table 2 illustrates several additional points. Control preparations showed that E46$^+$ alone gave the expected pattern of neutralization by Ad. 7 but not Ad. 2 antiserum, and that passage of Ad. 2 alone in AGMK did not result in its acquisition of SV40 neoantigen-inducing capacity. In experiment 2, the ability of E46$^+$ to donate the SV40 genetic material was compared with that of SV40 virus. In contrast to the ready hybridization of Ad. 2 by E46$^+$, a passage with SV40, either as a mixed infection or in cultures preinfected with SV40, did not yield detectable hybrid Ad. 2. This experiment also showed that E46$^+$ infection potentiated the growth of Ad. 2, analogous to the potentiation by SV40 infection.[9] In experiment 3 an attempt was made to rule out the possibility that some factor in the E46$^+$ virus pool other than Ad. 7 virus might be transferring the SV40 genetic material to Ad. 2. Rabbit antiserum to E46$^-$ virus, the nonhybrid Ad. 7 virus recovered from E46$^+$, was added to the E46$^+$-Ad. 2 mixture prior to inoculation into AGMK cultures; assay of the progeny of this infection indicated that no hybridization of Ad. 2 had occurred. It should be noted that the E46$^-$ virus used for the rabbit antiserum production is free of the 22 mμ viruslike particles found in most adenovirus preparations;[14] thus, if these particles were playing a role in the transfer of SV40 genetic material, the antiserum should not have prevented the hybridization.

Experiment 4 in Table 2 shows that transfer of the SV40 gene from Ad. 2$^+$ pool 1017 to Ad. 7 (E46$^-$) occurred as readily as did the initial transfer from E46$^+$ to Ad. 2.

Characterization of the hybridized Ad. 2: Several experiments were done to determine if the Ad. 2 virus which had acquired SV40 genetic material from E46$^+$ showed the distinctive biological characteristics of E46$^+$.[6-8] Pool 1017 was used in all studies. This pool titered $10^{7.0}$ pfu/0.1 ml in HEK cells, and $10^{4.8}$ $TCID_{50}$/0.1 ml in AGMK tube cultures. Undiluted virus inoculated into HEK coverslip cultures induced adenovirus neoantigen in 15.8 per cent of cells, and SV40 neoantigen in 10.7 per cent, and at other dilutions the percentage staining was directly pro-

TABLE 3

ULTRACENTRIFUGATION OF AD. 2 HYBRID

Material tested	Neoantigen Induction in HEK Cells: Per Cent Cells Positive, Ad. 12 HS*	Per Cent Cells Positive, SV40 HS	Ad./SV40 staining ratio
Starting material (pool 1017)	3.5	3.5	1.0
10,000 × *g* 1 Hr upper supernate	0.30	0.40	0.8
" lower supernate	0.53	0.40	1.3
" pellet (to volume)	2.0	2.2	0.9

* HS, tumored hamster serum.

TABLE 4

PROGENY RATIO TEST FOR DEFECTIVENESS OF AD. 2+ TITRATED IN HEK CELLS

Titration of Pool 1017: Dilution	Multiplicity (pfu/cell)	Day of harvest*	Assay of Harvest for Neoantigen induction in HEK, Per Cent Cells Stained: Ad. 12 HS	SV40 HS	Ad./SV40 staining ratio
10^{0}	$10^{1.5}$	4	15	50	0.3
10^{-1}	$10^{0.5}$	4	25	55	0.5
10^{-2}	$10^{-0.5}$	5	20	4.2	5
10^{-3}	$10^{-1.5}$	7	40	0.57	70
10^{-4}	$10^{-2.5}$	8	50	0.38	130
10^{-5}	$10^{-3.5}$	9	70	0.02	3500
10^{-6}	$10^{-4.5}$	10	70	<0.005	>14000
10^{-7}	$10^{-5.5}$	11	50	<0.005	>10000
10^{-8}	$10^{-6.5}$	Neg	..	...	...

* The titration tubes were harvested when cytopathic effects were complete, and the harvested fluids were assayed by inoculation of 0.1 ml of a 10^{-1} dilution into HEK coverslip dishes and fixing at 24 hr.

portional to concentration of inoculum. These percentages give estimates of virus titers of $10^{5.2}$/0.1 ml for adenovirus antigen-inducing particles, and $10^{5.0}$/0.1 ml for SV40 antigen-inducing particles.[6] There was no induction of antigen stainable with antiviral SV40 monkey serum. Thus, the hybrid Ad. 2 closely resembled E46+ in its 2 log higher infectivity titer in HEK than AGMK cells, the Ad./SV40 staining ratio of approximately one, the one hit dose-response relationship for neoantigen induction, and the inability to induce SV40 viral antigen.

Association of the SV40 gene with the Ad. 2 capsid was shown by the neutralization tests (Table 1) and by centrifugation studies (Table 3); as with E46+,[6] the ability to induce SV40 neoantigen sedimented with the adenovirus particles.

Defectiveness of the hybridized Ad. 2 particles was tested for by the procedures used in studies of E46+.[7, 8]

First, 8 plaque isolates of pool 1017 were obtained in HEK cell cultures; all were negative for SV40 neoantigen induction, and none could be passed serially in AGMK cultures. Second, defectiveness of the hybrid particles for HEK cells was further indicated by the progressive decline in proportion of hybrid particles in progeny of successive dilutions of a titration of pool 1017 in HEK cells (Table 4). This change of Ad./SV40 staining ratio with decreasing multiplicity of infection has been taken to indicate that dual infection of a cell is necessary for production of hybrid virus particles, while a single nonhybrid particle can initiate synthesis of nonhybrid adenovirus.[7] Third, plaque formation in AGMK cells followed a two-hit curve (Table 5), indicating that both the hybrid and nonhybrid particles are defective in these cells. As expected, the same pool titrated in HEK cells gave a dose-response relation compatible with one-hit kinetics.

Discussion.—The readiness with which the SV40 gene was transferred between adenoviruses strongly suggests that this gene is not linked with adenovirus genetic

TABLE 5

DOSE RESPONSE RELATIONS OF AD. 2+ POOL 1017 IN PLAQUE TITRATIONS IN AGMK AND HEK CELL CULTURES

	Number of Plaques*		
	AGMK		
Virus dilution	Titration #1	Titration #2	HEK
10^{-3}	265	TM	...
$10^{-3.5}$	30	250	...
10^{-4}	0	32	...
$10^{-4.5}$	0	...	...
10^{-5}	...	...	>464
10^{-6}	...	...	94
10^{-7}	...	...	12
Probability of occurrence[7] by:			
1-hit model	$\ll 0.001$	$\ll 0.001$	0.4
2-hit model	0.2	>0.05	$\ll 0.001$

* Total number of plaques on 2 dishes inoculated with 0.5 ml each. TM = Too many to count.

material in the "hybrid" particles, but is probably replicated separately, and randomly incorporated into adenovirus capsids. However, in the absence of comparable markers to detect exchange of adenovirus genes between serotypes, it cannot be ruled out that the SV40 gene is linked to a segment of adenovirus genetic material which is loosely linked with the remainder of the genome.

Although many adenovirus types have acquired SV40 genetic material as a consequence of either inadvertent[1, 4, 5] or deliberate[5, 15] passage with SV40 virus, the present studies and results of other workers[5, 16] indicate that acquisition of SV40 genes from this source is accomplished far less readily than from adenovirus donors. This observation suggests that in SV40 virus the gene for neoantigen induction may be tightly linked to the remainder of the SV40 genome, in contrast to the lack of linkage in the hybridized adenovirus particles. The defectiveness of the Ad. 2 "hybrid" particles provides further evidence that either the adenovirus capsid cannot accommodate both the SV40 gene and the complete adenovirus genome or that the process of encapsidation is such that simultaneous incorporation of both genetic materials is a rare event.

Conclusions similar to those reported here have been reached independently by Rapp, Butel, and Melnick[17] based on recent studies from their laboratory.

Summary.—Mixed infection of AGMK cultures with a "hybrid" and a nonhybrid adenovirus type yields comparable amounts of "hybrid" virus of both serotypes. The SV40 gene was transferred from Ad. 7 strain E46+ to adenovirus types 2, 4, 5, and 12, and from the artificially created Ad. 2 "hybrid" to E46−. The mixed infection with "hybrid" Ad. 7 potentiated the growth of the nonhybrid adenovirus comparable to the potentiation by SV40 virus.

Mr. Wendell E. Pugh rendered excellent technical assistance.

* This work was supported in part by the National Cancer Institute.

† Parts I and II of this series of studies of adenovirus-SV40 hybrid viruses may be found in the *Journal of Experimental Medicine*.[6, 7]

[1] Huebner, R. J., R. M. Chanock, B. A. Rubin, and M. J. Casey, these PROCEEDINGS, **52**, 1333 (1964).

[2] Rowe, W. P., and S. G. Baum, these PROCEEDINGS, **52**, 1340 (1964).

[3] Rapp, F., J. L. Melnick, J. S. Butel, and T. Kitahara, these PROCEEDINGS, **52**, 1348 (1964).

[4] Easton, J. M., D. E. Moore, and C. W. Hiatt, *Federation Proc.*, **24**, 174 (1965).

[5] Lewis, A. M., Jr., S. G. Baum, K. O. Prigge, and W. P. Rowe, unpublished data; Huebner, R. J., and A. J. Morris, personal communication.

[6] Rowe, W. P., S. G. Baum, W. E. Pugh, and M. D. Hoggan, *J. Exptl. Med.*, in press.

[7] Rowe, W. P., and S. G. Baum, *J. Exptl. Med.*, in press.

[8] Boeyé, A., J. L. Melnick, and F. Rapp, *Virology*, **26**, 511 (1965).

[9] Rabson, A. S., G. T. O'Conor, I. K. Berezesky, and F. J. Paul, *Proc. Soc. Exptl. Biol. Med.*, **116**, 187 (1964).

[10] O'Conor, G. T., A. S. Rabson, R. A. Malmgren, I. K. Berezesky, and F. J. Paul, *J. Natl. Cancer Inst.*, **34**, 679 (1965).

[11] Rowe, W. P., J. W. Hartley, and R. J. Huebner, *Proc. Soc. Exptl. Biol. Med.*, **97**, 465 (1958).

[12] Rowe, W. P., R. J. Huebner, J. W. Hartley, T. G. Ward, and R. H. Parrott, *Am. J. Hyg.*, **61**, 197 (1955).

[13] Pope, J. H., and W. P. Rowe, *J. Exptl. Med.*, **120**, 121 (1964).

[14] Hoggan, M. D., *Federation Proc.*, **24**, 248 (1965); Atchison, R. W., B. C. Casto, W. McD. Hammond, *Science*, **149**, 754(1965); Melnick, J. L., H. D. Mayor, K. Smith, and F. Rapp, personal communication.

[15] Schell, K., and R. J. Huebner, personal communication.

[16] Rapp, F., and L. A. Feldman, personal communication.

[17] Rapp, F., J. S. Butel, and J. L. Melnick, these PROCEEDINGS, **54**, 717 (1965).

---

*SV40-ADENOVIRUS "HYBRID" POPULATIONS: TRANSFER OF SV40 DETERMINANTS FROM ONE TYPE OF ADENOVIRUS TO ANOTHER**

BY FRED RAPP, JANET S. BUTEL, AND JOSEPH L. MELNICK

DEPARTMENT OF VIROLOGY AND EPIDEMIOLOGY, BAYLOR UNIVERSITY COLLEGE OF MEDICINE, HOUSTON, TEXAS

Communicated by R. J. Huebner, July 30, 1965

Recent reports have documented the existence of an adenovirus type 7 strain (stocks E46 and SP2) which can induce the synthesis of papovavirus SV40 tumor, or T, antigen in green monkey kidney (GMK) cells, or in tumors induced in hamsters by this adenovirus population.[1-3] (This antigen was discovered by Huebner who named it the tumor or T antigen. It has since been referred to as INCA, ICFA, or NEO. To avoid the tendency of each new worker introducing his own "exotica," we have continued to use the original model T terminology. It has the advantage of priority and simplicity, and furthermore, regardless of whether present in tumor cells or in virus-infected cells, the T antigen thus far can be detected only by using antibodies present in tumor-bearing animals.) The antigens induced by this adenovirus are similar or identical to those present in GMK cells during the early phases of the SV40 cytolytic cycle[4-7] and to those synthesized in all cells transformed by SV40.[8-10] SV40 viral antigens or infectious SV40 are never detected, and both the *in vitro* and *in vivo* SV40-related activities of the SP2 stock can be abolished by neutralization with adenovirus type 7 antiserum.[1-3] It was therefore postulated that during a previous joint infection, the adenovirus 7 had incorporated a portion of the SV40 genome into its own.

Although SV40 enhances the growth of adenoviruses in GMK cells,[11-14] the SP2 strain of adenovirus 7 grows equally well in GMK cells in either the presence or absence of SV40.[13] However, the SV40 tumor antigen determinant is lost after