Tumor Resistance and Tumor Enhancement with SV$_{40}$ Virus-induced Tumors

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SV$_{40}$ virus-induced tumors and cell cultures transformed by this virus possess new antigens. One antigen studied extensively has been the induced complement-fixation antigen, designated as SV$_{40}$ “T” or neoantigen (Black et al., 1963; Rapp et al., 1964; Sabin et al., 1964; Habel et al., 1965; Gilden et al., 1965). The antigen can be detected by immunofluorescence techniques as described by Pope and Rowe (1964) employing sera from hamsters bearing noninfectious SV$_{40}$-induced tumor transplants. In addition to the antigen measured by the complement-fixation (CF) reaction, evidence exists which points to the presence of cellular antigen(s) which are highly effective in promoting development of tumor resistance. This report is concerned with this latter type of antigen.

By way of a quick review, previous studies with transplantable polyoma and SV$_{40}$-induced tumors in hamsters and mice revealed the presence of a new, foreign antigen which is specific and of the “homograft” type, being demonstrable by resistance to tumor transplant challenge (Habel, 1961; Sjögren, Hellström, and Klein, 1961; Habel and Eddy, 1963; Koch and Sabin, 1963; Defendi, 1963). In these studies adult hamsters received immunizing inocula of either SV$_{40}$ or polyoma virus and were found to be resistant to challenge with homologous tumor cells. The hypothesis proposed that transformed cells, but not tumors, developed in vivo as a result of virus inoculation in adults. These cells, in turn, produced an antigen which was responsible for development of resistance.

Other studies indicated that SV$_{40}$ induced hamster tumors, and cell cultures prepared from such tumors (X-irradiated before use), were highly effective in preventing the occurrence of SV$_{40}$ tumors (Goldner, Girardi, Larsen, and Hilleman, 1964). In those studies the virus was inoculated into newborn hamsters and the immunizing cell preparations were injected during the latent period prior to the appearance of tumors. Virus used during the latent period was also effective for inducing tumor resistance (Eddy, Grubbs, and Young, 1964; Deichman and Kuchareva, 1964).

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*Human* cell cultures transformed by SV$_{40}$ similarly possess the CF neoantigen as described for hamster tumors and this antigen continues to be produced long after the cells cease to shed infectious virus (HABEL, JENSEN, PAGANO, and KOPROWSKI, 1965; GIRARDI, JENSEN, and KOPROWSKI, 1965). Furthermore, the transformed human cells were very effective in preventing SV$_{40}$ virus oncogenesis in hamsters even though the cells are of a species foreign to the experimental host (GIRARDI, 1965).

**Materials and Methods**

In the experiments to be described, newborn hamsters received SV$_{40}$ via the subcutaneous route. If untreated, tumors begin to appear 3 to 4 months later and eventually almost 100% of the animals develop tumors. However, in our studies, during the latent period, prior to the appearance of tumors, each litter was subdivided for immunization or for use as untreated or placebo controls. The immunizing inocula consisted of whole cells, or extracts of cells prepared as described in the text and were given as single doses via the intraperitoneal route. Animals were then followed for development of the SV$_{40}$ induced tumors.

**Results**

The results in Fig. 1 are typical of our studies with SV$_{40}$-transformed human cells. In this experiment SV$_{40}$ virus was given to newborn hamsters and on day 60 each litter was subdivided in 3 groups. One group received no further treatment, the other two groups received $8 \times 10^6$ whole cells from SV$_{40}$-transformed human cultures selected from 2 different times of the cells transformation cycle. "Crisis" is an event which takes place after virus transformation but before the human cell cultures have become permanently established lines. It is characterized by progressive decline in vigor of culture proliferation, increasingly abnormal cell division and finally massive degeneration of the cultures (GIRARDI, JENSEN, and KOPROWSKI, 1965). However, during crisis a small number of cells survive and give rise to a population capable of indefinite propagation. It is apparent from Fig. 1 that intact cells before and after crisis are effective for inducing tumor resistance. Experiments of this type have been repeated many times with similar results.