Tobacco Necrosis Virus and its Satellite Virus

In a recent letter[1] Grogan and Uyemoto reported that they were unable to obtain cultures of tobacco necrosis virus (TNV) free from satellite virus (SV) after repeated isolation of single lesions from mixed inocula, and they quote Kassanis and Nixon[2] as having the same experience. I write to point out that the paper quoted gives evidence to the contrary. It even shows photographic evidence of a gel-diffusion test to prove that when TNV is inoculated alone SV is not produced. Indeed, the fact that the Rothamsted tobacco necrosis virus contained two viruses and not two components of one, as previously seemed likely[3], became evident when a culture of the same tobacco necrosis virus was found free from the other component[4], now recognized as satellite virus. The different strains of TNV used in all subsequent work[5–7] were free from SV and remained so as long as the plants in which they were propagated were grown in uninfested soil.

I have received many isolates of TNV from many countries and most have been free from SV but able to activate SV when mixed with it. Indeed, only a few from the United Kingdom and Holland were accompanied by SV. Grogan and Uyemoto's conclusion that SV is always produced during multiplication of TNV is therefore not true.

Last year[8] I reported a second strain of SV (SV_2) serologically very different from the original (SV_1). The two satellite viruses can be activated by three different strains of TNV belonging to the two serotype groups of TNV, but the antigenicity of SV is not influenced by that of TNV. Perhaps the two satellite viruses reported by Grogan and Uyemoto are activated only by specific strains of TNV, but until their TNV cultures are freed from SV and the appropriate mixtures tested no conclusion is possible.

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Mutants of Simian Virus 40 which differ in Cell-transforming Activity

The hamster tumour A_4 26 induced by simian virus 40 ($SV40$), in contrast to most other hamster tumours induced by $SV40$, yields consistently small amounts of infectious $SV40$ (ref. 1).

During the course of these investigations it was observed that virus isolated from the tumour A_4 26 produced in all instances small to minute plaques, while the laboratory strain 777 gave rise to large plaques which were easy to recognize. Addition of DEAE–'Dextran' to the overlay had no effect on the plaque size.

The small plaque virus (SP) derived from tumour A_4 26 and the large plaque virus (LP) derived from strain 777 were plaque purified, and the properties of the respective clones were studied. The results are given here.

LP and SP appeared genetically stable in so far as SP never yielded LP and vice versa. The average diameter of plaques 24 days after inoculation was 10 mm for LP and 2 mm for SP. LP and SP adsorbed equally well to African green monkey kidney cells.

In single cycle growth curves, using an input multiplicity of ten, the multiplication of LP could first be detected after 24 h, that of SP after 30 h after inoculation. The rates of multiplication were similar for both mutants and decreased in both cases 48 h after inoculation. The final yields per cell were 5,000 plaque forming units (P.F.U.) for LP and 70 P.F.U. for SP. More SP remained associated with cells than did LP. These findings may explain the differences in plaque size.

While the amounts of virus synthesized during a single growth cycle differ markedly for LP and SP, no such difference was found for the amount of neoantigen (tumour antigen) produced by either of the two viruses.

The ratio of physical particles to P.F.U. was about 200 for LP and 600 for SP.

Cross-neutralization tests revealed no antigenic differences between LP and SP, but the SP was less readily neutralized.

On heating to 56° C the infectivity of SP was markedly more stable than that of LP (about thirty times). In both cases the kinetics of inactivation were not of first order.

The transforming capacity of SP was more than 200 times greater than that of LP as determined by transformation of primary weanling hamster kidney cells. The evidence so far obtained indicates that tumour cells induced by SP may again be virogenic, while LP tumour cells do not yield infectious virus.

When SP was inoculated in BS-C-1 cells[2] it was found that after the initial, almost complete destruction of the cell sheets the few surviving cells could be serially propagated. During the course of more than twenty passages such cultures never showed any cytopathic effect, although SP production could consistently be demonstrated (10^4–10^6 P.F.U./ml. of culture fluid).

The relation of the mutants described here to the $SV40$ variants of Altstein *et al.*[3] and Takemoto *et al.*[4] remains to be established.

The bases for the different virus-cell relationships and the different oncogenic potentialities of these mutants are being investigated at present. Furthermore, the high yields of virus which can be obtained with LP will make possible a thorough investigation of the virus structure.

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IMMUNOLOGY

Protective Effect of Anti-lymphocytic Serum on Murine Lymphocytic Choriomeningitis

Lymphocytic choriomeningitis (LCM) virus inoculated intracerebrally into mice produces a disease that is usually fatal. Such infections are, however, rarely fatal in mice that have been X-irradiated[1,2] or treated with radiomimetic drugs[3], although they carry the virus in high concentration indefinitely. These and other observations suggested that the lethal disease results from a hypersensitive reaction against the virus or against some product of the virus[4,5], and certain evidence seems to implicate cells of the central nervous system in this reaction[6]. Congenitally infected mice do not develop acute illness, although they maintain high levels of viraemia throughout their lives[7]. When such mice are inoculated with adequate numbers of histo-compatible lymphocytes from immunized