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Letter

Origin of nine base pair duplication in the 3′ terminus of the SV40 T-Ag gene

Newman *et al*, 1998 identified SV40 DNA in healthy and SIV-infected rhesus monkeys. Relative to strain 776 wtSV40 DNA they described a 9 bp reiteration and a T to C nucleotide substitution in the 3′ terminal region of the T-Ag gene, the host range domain (HRD). They compared their findings to studies where SV40 DNA was identified in several human tumors in which the same nucleotide differences were observed (Table 5 and Ilyinskii *et al*, 1992; Lednicky *et al*, 1995; 1997a,b; Stewart *et al*, 1996).

In several reports in the late 1970s and early 1980s, we demonstrated that the large plaque strain of wtSV40 (triple plaque purified) propagated in human fetal spongioblasts and several human tumor cell lines, including A172 glioblastoma cells (Carroll and O'Neill, 1978; O'Neill and Carroll, 1978, 1981; O'Neill *et al*, 1982). After SV40 growth in A172 cells, several alterations in the transcriptional control region (TCR) appeared, along with defective interfering (DI) viral DNAs. The DIs appeared rapidly and often contained either the entire early region or the entire late region but nearly all of the remaining coding sequences were deleted. In addition, the TCR and the terminus region, which contains the HRD, were triplicated. In 1993 (O'Neill *et al*), we reported the DNA sequence of the E-SV40 variant. We showed the positions of several rearrangements, base substitutions and deletions. We discovered what first appeared as a 9 bp insertion (8 bp at one position and another bp at a nearby position) between nucleotides 2780 and 2783. In addition, the T to C transition at nucleotide 2792, while also absent form large plaque SV40 DNA, was observed but not reported. However, when we aligned our DNA sequence (Figure 1) with that shown by Newman *et al*, (1998) we found that our 9 bp duplication was identical with those shown by Newman *et al*. (1998). Because the 9 bp 2790–2782 sequence can be triplicated (Figure 5, Newman *et al* 1998), the 9 bp reiteration from 2790–2782 we believe correctly describes our variant.

Most importantly, the appearance of these alterations in SV40 DNA suggests that such variants can develop rapidly after infection of some neural cells, and therefore may be generated in individual simians or humans originally infected with other strains of virus. Also, because some of the alterations in SV40 DNA occur in cultured human neural cells, including those in the HRD region, indicates that the SV40-neural cell culture may be a reflection of SV40 diversity occurring in primates. These problems are being investigated.

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	2793	2779
Strain 776	GTCCTCACAGTC----------	TGT
Newman *et al.* 1998	G**C**CCTCACAGTCCTCACAGTC----------	TGT
E-SV40 (O'Neill *et al.* 1993)	G**C**CCTCACAGTCCTCACAGTC----------	TGT
SV40-B2	G**C**CCTCACAGTCCTCACAGTC----------	TGT
Gang. 13	G**C**CCTCACAGTCCTCACAGTC----------	TGT
Ost. 2	G**C**CCTCACAG**C**CCTCACAGTCCTCACAGTCTTGT	
Ost. 9	G**C**CCTCACAGTCCTCACAGTCCTCACAGTCTTGT	

Figure 1 (Modified from Figure 5 of Newman *et al*, 1998)