**Simian Virus 40 (SV40) and Human Cancers**

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**Abstract**

Simian virus 40 (SV40) contaminated the early poliovirus vaccines used throughout much of the world during the late 1950s and early 1960s. SV40 is oncogenic in rodents and can transform human cells in vitro. Most epidemiologic studies, however, have failed to detect increased risks of cancer among those exposed to SV40-contaminated poliovirus vaccines, even after more than 30 years of follow-up. In contrast, an increasing number of recent DNA hybridization studies have reported detection of SV40 genomic sequences in human tumors. The majority of these reports have involved ependymoma, choroid plexus tumors, osteosarcomas, and mesotheliomas. Not all investigations have detected SV40 in human tissues, though, and even among positive studies, several factors such as the low levels of virus found in tumors (<1 genome copy per tumor cell), raise uncertainties regarding the possible role of SV40 in human cancers. This review article briefly summarizes the evidence for and against recent assertions that SV40 is a human tumor virus.

**Introduction**

Simian virus 40 (SV40) was an inadvertent contaminant of the early poliovirus vaccines used throughout much of the world during the late 1950s and early 1960s. Hundreds of millions of people were immunized with SV40-contaminated vaccine, making this by far the largest single-source exposure to SV40 in humans. SV40 is oncogenic in rodents and can transform human cells in vitro. Consequently, cancer was the primary concern of scientists and public health officials initially investigating the effects of SV40 exposure in humans. Most epidemiologic studies, however, have failed to detect increased risks of tumors in groups immunized with SV40-contaminated poliovirus vaccines. Attention to this topic waned. Then in 1992, SV40 genomic sequences were detected in human tissues, though, and even among positive studies, several factors such as the low levels of virus found in tumors (<1 genome copy per tumor cell), raise uncertainties regarding the possible role of SV40 in human tumors. Additionally, more than 30 years following the contamination of poliovirus vaccines with SV40, updated epidemiologic analyses, now focused on the tumors reported to contain SV40 DNA, have not detected increased rates of cancers in exposed birth cohorts. Many physicians and scientists may be unfamiliar with these issues. Therefore, this review article is meant to provide a summary of the SV40 literature, as well as the controversies surrounding the possible association of SV40 with the development of tumors in humans.

**Human Exposure to SV40**

SV40 is a common asymptomatic infection of Asian macaques. Classified as a polyomavirus, a group of small, non-enveloped, double-stranded DNA viruses, SV40 has substantial genomic, antigenic and biologic similarities to the known human polyomaviruses, BK and JC viruses. Each of these viruses is tropic for renal epithelial cells (Melnick et al., 1974; Hogan et al., 1991; Cole, 1996).

Contamination of the early poliovirus vaccines with SV40 occurred because rhesus and cynomolgus monkey kidney cell cultures were used to grow poliovirus during vaccine preparation (Shah and Nathanson, 1976; Hilleman, 1998). This contamination initially went undetected since SV40 does not induce discernable cytopathologic changes in renal cells from its natural hosts. Not until 1960, when culturing in cells of a heterologous monkey species was observed to result in vacuolization and cell death, was this previously unknown virus discovered (Sweet and Hilleman, 1960; Hilleman, 1998). In 1961, it was found that injection of SV40 at high titer could induce tumors in recently born rodents (Eddy et al., 1961; Eddy, 1962). That same year the United States government required that all new lots of poliovirus vaccine be free of SV40, but earlier lots were not withdrawn from the mass immunization program. Overall, SV40-contaminated vaccine was probably in widespread use in the United States from the beginning of the mass immunization program in 1955 through early 1963. SV40 contamination also affected early adenovirus vaccine preparations, but this exposure was relatively limited, involving mainly military recruits. Worldwide, during the late 1950s and early 1960s, hundreds of millions of individuals were immunized with poliovirus vaccines contaminated with SV40 (Shah and Nathanson, 1976).

The level of live SV40 in poliovirus vaccines varied considerably. The formalin concentrations used to inactivate poliovirus also inactivate SV40, but not as completely (Gerber et al., 1961). Therefore, the inactivated poliovirus vaccine (IPV) utilized by the mass immunization program in the United States probably contained mostly low SV40 viral titers. The live-attenuated oral poliovirus vaccine (OPV), used widely in Europe, contained mostly high SV40 titers (Shah and Nathanson, 1976). Whether
human infection resulted from IPV or OPV related exposure to SV40 is not entirely known, however. Contaminated OPV did not induce SV40 antibodies in vaccinees, and studies to detect shedding of SV40 in stool had conflicting results (Sweet and Hilleman, 1960; Goffe et al., 1961; Magrath et al., 1961; Melnick and Steinbaugh, 1962). In contrast, injection with contaminated IPV did induce antibodies to SV40, but whether this reflected SV40 infection or simply an immune response to viral antigens is unclear (Gerber, 1967). No attempts to isolate SV40 from IPV recipients were ever reported. The best evidence that SV40 can, at least under certain circumstances, infect humans comes from a study by Morris et al. (1961). Adult volunteers received an inhaled aerosol that, like the poliovirus vaccine, had been inadvertently contaminated with SV40. Seroconversion to SV40 was observed in 22 of 35 subjects, and the virus was successfully isolated from throat swabs in three of eight subjects tested several days following exposure.

Epidemiologic Investigations

A number of epidemiologic investigations have studied the risks of cancer in populations immunized with SV40-contaminated poliovirus vaccine (Strickler and Goedert, 1998). The first investigation by Fraumeni et al. (1963) examined national cancer mortality rates among the millions of children 6-8 years of age in the United States immunized with IPV during 1955, the first vaccines of the mass immunization program. The investigators compared children according to the level of live SV40 in the vaccines they received, categorized as high, low, or no SV40 based on tests of stored specimens. Four years following vaccination, no relation between SV40 virus exposure and cancer mortality was detected.

Longer follow-up studies similarly failed to show any relationship between risks of cancer and exposure to SV40-contaminated poliovirus vaccine. Mortimer et al. (1981) followed children for 17-19 years who had participated in a study involving poliovirus vaccination during the first days of life, the most vulnerable period for exposure to SV40 according to animal models. Although the vaccines used were later confirmed to contain high levels of live SV40, only one tumor, less than the number expected, and no evidence of other adverse health consequences, were observed. In Germany, Geissler et al. (1990) reported more than 22 years of follow-up data on 885,783 children born 1959-1961 who were exposed to SV40-contaminated vaccine. As compared with unexposed children, born just a few years later, no increased risks of cancer were observed. These negative results included several tumors that were later reported to contain SV40 DNA, including ependymoma, choroid plexus tumors, medulloblastoma, and glioma.

To more comprehensively study the tumors reported to contain SV40, we recently conducted a large, long-term retrospective follow-up study of birth cohorts exposed or unexposed to SV40-contaminated poliovirus vaccine (Strickler et al., 1998). The tumors investigated included ependymoma, all brain cancers combined, osteosarcoma, and mesothelioma. More than 30 years of follow-up data were available. The analyses found that those exposed to SV40-contaminated poliovirus vaccine as infants, born 1956 through 1962 (60,811,730 person-years of observations) or as children, born 1947 through 1952 (46,430,953 person-years) did not have increased risks of cancer relative to unexposed birth cohorts, born 1964 through 1969 (44,959,979 person-years). Additional analyses found that the exposed birth cohorts also did not have increased risks of medulloblastoma (Strickler et al., 1999), non-Hodgkin's lymphoma, leukemia, ovarian cancer, or all cancers combined (unpublished results). In a recent study from Sweden, consistent with the United States data, investigators reported that there was no relationship between exposure of infants or children to SV40-contaminated poliovirus vaccines and risks of ependymoma, all brain cancers, osteosarcoma, or mesothelioma (Olin and Giesecke, 1997).

Only two case-control investigations have been reported, and these provided conflicting results. A case-control study in Australia found a small increased probability of having received IPV (88%) among childhood cancer cases than in matched controls (81%) (Innis, 1968); however, a similar study conducted in England failed to confirm this relationship (Stewart and Hewitt, 1965). More concerning findings were obtained in the only two studies of in utero exposure to SV40, referring to maternal vaccination with SV40-contaminated vaccine during pregnancy (Heinonen et al., 1973; Farwell et al., 1979). In both investigations, increased risks of tumors of neural origin were observed among exposed offspring. The tumors associated with in utero SV40 exposure, however, were different in each study. Medulloblastoma risk was increased in the first study (Farwell et al., 1979), and neuroblastoma, which is not a central nervous system tumor, in the second study (Heinonen et al., 1973). Additional limitations to these investigations have been reported (Strickler and Goedert, 1998). Nonetheless, these troubling results do require further investigation.

In summary, most epidemiologic studies to date have failed to suggest an association between the contamination of the early poliovirus vaccines with SV40 and subsequent rates of cancers in the United States and Europe. The exposed birth cohorts are still young (most are less than 50 years of age), and must continue to be monitored for adverse health outcomes that may only be observed later in life, (mesothelioma, in particular), or that might require longer follow-up to be detected. More research also needs to be done to determine the risks of cancer among individuals potentially exposed in utero.

Detection of SV40 in Human Cancers

In contrast with most epidemiologic investigations, DNA hybridization studies increasingly suggest a possible relation of SV40 with human cancers. Most of these reports have involved ependymoma, choroid plexus tumors, osteosarcoma, and pleural mesothelioma. Bergsagel et al. (1992) reported the important initial findings. Using PCR, the investigators detected SV40 DNA in 10 of 20 choroid plexus tumors and 10 of 11 ependymomas. No SV40 DNA was detected in any of over 100 normal
blood samples tested or 12 neuroblastomas, although 1 of 7 normal brain specimens obtained from a premature infant was positive. Repeat testing of these same tissues in an independent laboratory confirmed the presence of SV40 in the ependymoma and choroid plexus tumors, and further revealed that DNA sequences from several different regions of the SV40 genome could be amplified (Lednicky et al., 1995). Most importantly, infectious SV40 was successfully isolated from one choroid plexus tumor (Lednicky et al., 1995).

A number of subsequent PCR studies have reproduced the detection of SV40 DNA in ependymoma and choroid plexus tumors, and have also found the virus in additional central nervous system neoplasms. Martini et al. detected SV40 DNA in most choroid plexus tumors, ependymomas, astrocytomas, and glioblastomas, as well as in several meningiomas. None of 13 normal brain specimens was positive (Martini et al., 1996). Unexpectedly, though, 45% of normal sperm specimens and 23% of peripheral blood specimens were also positive for SV40. Even more curious, every SV40 positive specimen was additionally positive for BKV DNA. In more recent studies, Huang et al. (1999) found SV40 DNA in a high proportion of many of these same central nervous system tumors, but found BKV and JCV to be at low prevalence (<3% of samples). Similarly, Zhen et al. (1999) found SV40 DNA in a wide range of central nervous system tumors but not in normal brain, using a novel assay for detection of SV40 large T antigen (Tag).

Human osteosarcoma was first reported to contain SV40 DNA by Carbone and colleagues (1996). In an initial survey, 18 of 151 various tumors from Li-Fraumeni patients were positive for SV40 DNA by PCR, and most of the positive tumors were noted to be osteosarcomas. Further tests found 35 of 111 additional osteosarcomas and 14 of 34 other bone tumors positive for SV40. Lednicky et al. (1999) replicated these findings, detecting SV40 DNA in 5 of 10 osteosarcomas by PCR. In that study, several different regions of the SV40 genome were amplified from specimens, and there was virus sequence variation between the tumors, findings which the investigators stated made contamination an unlikely explanation for the results. Mendoza et al. (1998) detected SV40 DNA in osteosarcomas using Northern blot without prior DNA amplification, the very first study to detect SV40 in human tissues in such a manner. This is important, as non-amplification assays are less prone to false positive results. In addition, these investigators found that the SV40 sequences in tumors were integrated into the host DNA, findings consistent with in vitro and animal studies of SV40 and cancer. As pointed out by Shah, however, several aspects of the results were difficult to explain (Shah, 2000). First, BKV DNA was detected at even higher prevalence than SV40. Second, in one case the primary tumor was positive for SV40 DNA but the recurrent tumor was not. Last, in one patient, integrated SV40 DNA was unexpectedly detected in normal as well as in two tumor specimens and, moreover, the integration pattern was different in each of these specimens (Mendoza et al., 1998).

Mesotheliomas have been the most extensively studied of the tumors reported to contain SV40 DNA. In the first report, 29 of 48 mesothelioma specimens were found to contain SV40 DNA sequences (Carbone et al., 1994). Among the additional specimens tested, 1 of 7 squamous cell lung carcinomas, 1 of 6 gastric cancers, but none of 13 lung adenocarcinomas or 14 normal lung specimens were SV40 positive. Surprisingly, SV40 Tag protein was detected by immunohistochemistry and immunoprecipitation in most mesothelioma specimens tested, including SV40 PCR-negative tumors. No relation was found between detection of SV40 and detection of asbestos fibers, the principal risk factor for development of mesothelioma.

The detection of SV40 DNA in mesotheliomas has since been replicated in a number of studies: Cristaudo et al. (1996) found SV40 DNA in 8 of 11 mesotheliomas as compared with 0 of 6 normal blood samples; Pepper et al. (1996) detected the virus in 4 of 9 mesotheliomas as opposed to 0 of 9 lung adenocarcinomas or 3 reactive pleural specimens; and Gallateu-Salle et al. (1998) reported SV40 DNA in 10 of 21 mesothelioma specimens and in 18 of 63 lung cancers, as compared with 4 of 25 normal human lung specimens. Of particular interest, a multi-institutional study conducted with the stated purpose, “to conclusively determine the presence or absence of SV40 in human mesotheliomas” (Testa et al., 1998). In that study, 12 tumors were obtained from an independent medical center. The tumor DNA was extracted at a single test site, and then tested in four independent laboratories, each using two separate PCR assays. SV40 was found in most tumors in each of the laboratories, with three laboratories detecting SV40 DNA in all specimens in at least one PCR assay. These data raise concerns, though, because SV40 DNA is not expected in 100% of mesotheliomas. In addition, high prevalence but varied detection of viral DNA can be consistent with low level contamination. Moreover, since no normal tissues or SV40-negative cell lines were tested, the possibility of contamination (e.g., during tissue processing) was not adequately addressed. Stronger evidence that SV40 may be present in some mesotheliomas has been provided by a more recent study. Specifically, following microdissection, Shivapurkar et al. (1999) detected SV40 DNA in samples extracted from tumor cells but not in adjacent non-tumor tissues, results that can not as readily be explained by contamination.

**Biologic Plausibility**

Several sources of evidence suggest that a relationship between SV40 and cancer in humans is biologically plausible. It has already been mentioned that SV40 can induce tumors in neonatal rodents and, strikingly, these tumors include several, such as ependymomas, osteosarcomas, and mesotheliomas, which have been reported to contain SV40 DNA in humans (Hogan et al., 1991). Moreover, SV40 can transform human cells in vitro (Kaprowski et al., 1962), and likely mechanisms by which this occurs have been extensively described (Kim et al., 1998; Rundell et al., 1998). In brief, SV40 Tag is known to bind and inactivate the tumor suppressor proteins p53 and Rb, as well as additional regulator proteins in control of the cell cycle. In keeping with this, it has been reported that the presence of
SV40 Tag in mesothelioma specimens is associated with the detection of p53, and that the two proteins co-precipitate, suggesting their physical association in these cells (Carbone et al., 1997). Tag extracted from mesotheliomas was also found to bind several proteins of the Rb family in vitro (De Luca et al., 1997). Evidence that Tag expression can directly affect the growth arrest and apoptosis in SV40-positive mesothelioma cell lines, whereas no such effect occurred in cell lines negative for SV40 (Waheed et al., 1999).

**Uncertainties Regarding the Role of SV40 in Human Cancers**

The failure of most epidemiologic investigations to detect a relationship between cancer rates and the period of SV40-contamination of poliovirus vaccines, the largest single source exposure to SV40 in humans, is important evidence inconsistent with the putative role of SV40 in human tumors. As discussed above, each of the several large, long term cohort studies of this topic had negative results. The purpose of this section is to summarize several additional sources of current skepticism towards recent assertions that SV40 is a human tumor virus.

1) Many SV40 DNA positive tumors, such as ependymoma or osteosarcoma, have been detected in children too young to have received contaminated poliovirus vaccines. For this to be correct, SV40 must be actively circulating in the general population, and transmitted person-to-person. Polyomaviruses, however, are highly species-specific, inconsistent with such a possibility (Shah, 2000). Direct evidence regarding the presence of SV40 in human communities is limited and conflicting. Shah et al. tested urine samples from HIV-positive and -negative homosexual men for polyomaviruses (Shah et al., 1997). High prevalence of BK and JC virus DNA was observed, but no SV40. Investigators in Europe took the unusual step of testing sewage samples from several countries for polyomavirus sequences (Bofill-M as et al., 2000). High prevalences of BK and JC viruses were detected, but no specimens were positive for SV40. We tested patients with osteosarcoma, mesothelioma and normal controls using a well-characterized SV40 serum assay. Only a small number of low titer antibody responses were detected, consistent with cross-reactivity to human polyomaviruses. Two additional studies, however, had positive findings. Jafar et al. (1998) detected SV40 antibodies in 10-17% of HIV-positive and -negative homosexual men tested. These results are difficult to interpret, though, as SV40 seroprevalence was not significantly different (p=0.4; p-value not reported by authors) between individuals born during or after the period of SV40-contamination of poliovirus vaccines. It will be important, therefore, for these investigators to validate their seroassay. This could be done by testing subjects with known expected results, such as cases with SV40 DNA positive tumors, and appropriate negative controls. In a second study, Butel et al. (1999) reported detection of SV40 DNA in four tissues (3 transplanted kidneys and 1 Wilms’s tumor) of 20 SV40 seropositive children, each born after 1982. However, interpretation of this study is limited by the lack of an SV40 seronegative comparison group to confirm the specificity of the results. Overall, there is not strong evidence that SV40 is circulating and being transmitted in the general population.

2) Several studies did not find SV40 DNA sequences in human cancers. Krainer et al. (1995) failed to detect SV40 DNA in any of 10 ependymomas tested, even though amplification of the human β-globin gene, a measure of specimen adequacy, was positive, and their nested PCR assay was sensitive to fewer than 10 copies of the viral genome. Similarly, others failed to detect SV40 DNA in any of a series of ependymomas, choroid plexus tumors, glioblastomas, and other central nervous system tumors tested (De Mattei et al., 1994), and none of 10 meningiomas studies were positive for SV40 (Volter et al., 1998). In a comparatively large study, we detected SV40 DNA in none of 48 β-globin positive mesothelioma specimens, despite using two independent PCR assays targeted to different regions of SV40 Tag, each of which could detect 1-10 copies of the SV40 genome (Strickler et al., 1996). Additionally, as mentioned above, we also measured SV40 antibodies, but found only low titers in 3 of 34 mesothelioma cases, 1 of 33 osteosarcoma cases, and 1 of 35 normal controls, thought to reflect cross-reactivity with BKV and JCV (Strickler et al., 1996). Curiously, no other case-control investigations have reported results using SV40 seroassays. In one study, 0 of 12 -globin positive mesothelioma specimens were positive for SV40 DNA, despite using a PCR assay able to detect 1-10 copies of the viral genome (Mulatero et al., 1999). Recently, a large study had mostly negative findings. The investigators detected SV40 DNA in 1 of 25 ependymomas, 2 of 116 medulloblastomas, and 1 of 131 meningiomas. None of the few SV40-positive tumors expressed Tag, suggesting that were it true that occasional tumors contain SV40 DNA, the virus is, nonetheless, unlikely to play a role in tumorigenesis (Weggen et al., 2000).

3) Even among studies detecting SV40 DNA in human tumor specimens, major aspects of the data raise uncertainties regarding the possible role of SV40 in human cancers, especially when evaluated against the standard of several well-accepted tenets for establishing causality (Hill, 1965):

**Strength of Association—**Refers to detection of the agent in disease but not normal tissues. However, the high prevalence of SV40 DNA present in normal specimens, according to some recent reports, questions the virus’ strength of association with cancer. In particular, SV40 DNA was detected in 80% of normal pituitary samples (Woloschak et al., 1995), SV40 DNA was detected in 23% of normal blood and 45% of normal sperm specimens (Marti et al., 1996), and SV40 was found in 16% of normal lung specimens (Galateau-Salle et al., 1998).

**Specificity of Association—**Requires that a single cause lead to one and not multiple effects. In contradiction to this, experimental injection of high titers of SV40 in neonatal rodents can...
induce a wide range of neoplasms, raising the possibility that this virus could also cause a variety of tumors in humans (Hogan et al., 1991). Actual human exposure to much lower levels of SV40 through IPV, OPV or other sources, however, is less likely to have such broad effects. The list of tumors reported to contain SV40 DNA includes, tumors of the pituitary (Woloshak et al., 1995), thyroid (Pacini et al., 1998), squamous and anaplastic tumors of the lung (Carbone et al., 1994; Galateau-Salle et al., 1998), gastric cancer (Carbone et al., 1994), several types of bone tumors (Carbone et al., 1996), non-Hodgkin’s lymphoma (Martini et al., 1998; Rizzo et al., 1999), Hodgkin’s disease (Martini et al., 1998), lymphoproliferative diseases in immune compromised patients (Rizzo et al., 1999), as well as mesothelioma, osteosarcoma, ependymoma, choroid plexus tumors, medulloblastoma, glioma and other central nervous system neoplasms (as summarized above).

Biologic Plausibility—Several plausible biologic mechanisms by which SV40 may induce tumors have been described. However, most positive studies of SV40 DNA in human tumor specimens have found the virus at very low levels, probably involving only a fraction of cancer cells (Testa et al., 1998; Jasani, 1999). To explain this, proponents have postulated a “hit and run” mechanism, whereby the virus has an early effect but then is no longer needed once cancer has been established (Carbone et al., 1997). Such a mechanism has not been previously shown for any human tumor.

Temporality and Biologic Gradient—Temporality requires that exposure precedes development of disease. Biologic gradient requires that increased frequency or higher levels of exposure be associated with increased risks of disease. However, no evidence of temporality or a biologic gradient have been reported for the association of SV40 with human cancers.

As a whole, these observations suggest that even if SV40 is present in human tissues, it might not play an etiologic role in cancer. In keeping with this, studies by Geissler et al. found that SV40 preferentially infected cancer as compared with normal brain cells in rodents, following induction of central nervous system tumors by in utero ethyl nitrosoare (Geissler, 1990). Alternatively, several of the above observations (i.e., the high prevalence of SV40 in some normal tissues, the low levels of virus even in tumors, and the failure of several studies to detect SV40 in any human specimens) could also suggest some positive results are due to laboratory artifact. A number of observations are consistent with this possibility. First, positive PCR results have been difficult to confirm with less error prone non-amplification methods, such as Southern blot. Second, the risk of laboratory contamination with SV40 DNA is high. SV40 is one of the most widely used viruses, and investigators have reported that essentially all molecular laboratories have had exposure to SV40 viral sequences whether or not they have knowingly used the virus in their laboratories. That is, more than 200 vectors listed in EMBL and Genbank databanks are known to contain SV40 DNA sequences, encompassing all but a 286 nucleotide region of the viral genome (Volter et al., 1998). Last, problems with contamination have already been shown to exist. Stoner documented SV40 DNA contamination of nucleotides manufactured by a prominent vendor, leading to false positive results in his laboratory (Stoner, 1999). Difficulties with contaminated reagents were also described by Sangar et al. (Sangar et al., 1999) and, in other studies the investigators concluded that the detection of SV40 DNA in mesotheliomas in their laboratory was probably due to an artifact, since the least sensitive PCR assay gave the highest prevalence (Griffiths et al., 1998).

To better understand the many contradictory findings, we have recently completed a multi-institutional investigation with nine separate laboratories, including the majority that presented data (both positive and negative) at the recent international workshop titled, “Simian Virus 40 (SV40): A possible human pathogen” (Brown and Lewis, 1998). The results are currently being analyzed. When completed, this will be the first study to directly compare results in laboratories that reported conflicting findings. More importantly, it will also be the first study to assess intralaboratory reproducibility by using masked replicate mesothelioma samples, made indistinguishable from normal lung samples and control cell lines. Each laboratory used their own published assays, as well as one agreed to by all participants. In all, 15 separate PCR assays were conducted on each test specimen. The study addresses the questions: Does the same laboratory find the same tumor specimens positive each time tested? Are differences in laboratory results explained by differences in the sensitivity and specificity of their assays? What is the prevalence of SV40 in mesothelioma specimens among laboratories with reproducible, sensitive and specific assays? We expect the findings to be reported shortly.

Summary

More than 30 years after the widespread contamination of early poliovirus vaccines with SV40, it remains uncertain whether exposure to this oncogenic virus through immunization caused human infection or has resulted in any adverse health consequences. Most epidemiologic studies of humans exposed to SV40-contaminated poliovirus vaccine have failed to detect increased risks of cancer. However, an increasing number of PCR studies have reported the detection of SV40 DNA in human tumors. These include several tumors caused by SV40 experimentally in rodents. Evidence is mixed, though, regarding the detection of SV40 infection in the general population. Several studies have also failed to detect the virus in human tumors. Even among the positive studies, there are inconsistencies regarding the prevalence of SV40 DNA in normal tissues, and the very low levels of virus detected in tumors suggests that only a fraction of tumor cells probably contain viral sequences. An aggressive campaign to study the role of SV40 in human disease has been initiated, and despite the current uncertainties, it will almost certainly be known within the next few years whether SV40 is a human tumor virus.
References


