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Note

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Human Brain Tumors and Simian Virus 40

In early studies, simian virus 40 (SV40), a DNA tumor virus, was seldom detected in human tumors by use of Southern blot hybridization and/or immunohistochemical techniques [reviewed in (*1*)]. More recently, Bergsagel et al. (*2*) detected SV40 T antigen (Tag)-coding sequences with the polymerase chain reaction (PCR) in 10 of 20 choroid plexus papillomas and in 10 of 11 ependymomas, whereas Carbone et al. (*3*) found SV40 in 60% of human pleural mesotheliomas. We looked for SV40 Tag coding sequences in a variety of human brain specimens and in blood samples from healthy donors. We examined 58 primary brain tumors of different histotypes, 10 brain tumor-derived cell lines, 13 normal brain tissues, and 33 peripheral blood cell (PBC) samples. By using PCR followed by Southern blotting and hybridization with an oligomer probe specific for the SV40 early region, we found SV40 DNA sequences in five (83%) of six choroid plexus papillomas, eight (73%) of 11 ependymomas, three (43%) of seven astrocytomas, five (29%) of 17 glioblastomas, two (40%) of five glioblastoma multiforme-derived cell lines, and four (13%) of 30 PBC samples. None of the 13 normal brain tissues were positive for SV40 DNA, nor were seven meningiomas and one meningioma cell line, seven oligodendrogliomas, two spongioblastomas, one neuroblastoma, and four neuroblastoma cell lines. The two glioblastoma multiforme-derived cell lines that were positive for SV40 DNA showed expression of SV40 early-region sequences when analyzed by coupled reverse transcription and PCR, and SV40 Tag was detected by indirect immunofluorescence with the specific monoclonal antibody Pab 101. DNA sequencing of the amplification products from four brain tumor specimens (one ependymoma, one glioblastoma, and two glioblastoma multiforme-derived cell lines) confirmed that they were derived from SV40.

Our data indicate that SV40 Tag-coding sequences can be detected in a large variety of human neoplastic brain samples, suggesting that SV40 virus is more widespread in human neoplasms than reported before. It is interesting that SV40 early-region sequences were also detected for the first time in PBCs from healthy individuals used as control subjects. This result, in agreement with similar findings (*4,5*) of sequences from the human polyomaviruses BK (BKV) and JC (JCV), suggests that human PBCs may be vectors for the transfer of SV40 to other tissues. Because SV40 was not detected in normal brain specimens, the virus seems to be specifically associated, at least in human brain, only with neoplastic tissue. SV40 is oncogenic in rodents, and it is mutagenic and can transform human cells. Its oncogenicity is mainly related to the production of Tag, a transforming protein that is 85% homologous to BKV Tag. SV40 Tag induces extensive chromosome rearrangements, and it binds and inactivates the products of the p53 (also known as TP53) and RB tumor suppressor genes (*1*).

All specimens, brain tumors, and PBCs that were positive for SV40 sequences in this study were found in a previous investigation (*5*) to contain BKV sequences. This observation suggests that BKV could act as a helper virus for SV40 replication. Indeed, SV40 does not normally infect humans, and human cells are only semipermissive for the virus. SV40 has infected humans mainly through contaminated polio vaccines (*1*). Its multiplication in human cells and its circulation in the human population may have been helped by the ubiquitous BKV infecting the same host. In this way, SV40 could establish latent infections in specific human cells, exerting its oncogenic potential during the development or progression of brain tumors.

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Note

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Primary Extraskeletal Osteosarcoma—Experience With Chemotherapy

Extraskeletal osteosarcoma (EOS) is an extremely rare malignant neoplasm of soft tissues characterized by the production of osteoid or bone by the neoplastic cells (*1*). Primary EOS, unrelated to radiation therapy, is the subject of this correspondence. The traditional treatment for EOS has usually been