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Absence of SV40, BKV and JCV polyomaviruses in pediatric brain tumors and adrenocortical carcinomas.

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Germline p53 mutations are commonly observed in the Li-Fraumeni familial cancer syndrome (LFS), and are occasionally found in children diagnosed with component tumors of LFS including malignant brain tumors and adrenocortical carcinomas (ACC). Although somatic inactivation of the second (wild-type) allele, or loss of heterozygosity (LOH), frequently occurs, the wild-type allele is retained in approximately 40% of tumors. This suggests that other epigenetic mechanisms suppress wild-type p53 function. The SV40, BKV and JCV polyomaviruses express large T-antigen (Tag), which binds p53, inhibits p53-DNA binding, and abrogates transcriptional activation of downstream targets. We have previously shown that LFS patients express SV40 Tag in some tumors that are thought to be trophic for the virus, including choroid plexus tumors. BKV and JCV have also been linked to the development of a spectrum of human brain tumors. To further investigate the role of polyomaviruses in tumour development, we set out to determine the presence of SV40, JCV and BKV in 59 childhood brain tumor samples from our hospital and 10 adrenocortical carcinoma samples from Southern Brazil, in which the p53 mutation status was already known. The brain tumors included 8 medulloblastomas, 1 CPCs, 6 ependymomas, 17 tumors of glial cell origin, and 27 other histologic subtype. We employed a PCR-based method to amplify fragments of Tag with primers specific for SV40, BKV and JCV. DNA extracted from SV40-transformed COS7 cells, and from plasmids containing partial JCV and BKV Tag sequences were used as positive controls. A "touchdown" PCR technique was used to avoid nonspecific amplification. We duplicated the PCR reaction of each sample with the addition of 50ng positive control DNA to ensure the absence of inhibitory agents in the samples (neat and spike PCR). Amplified products were then resolved and visualized on a 3% agarose gel. None of the 69 samples demonstrated presence of the polyomavirus Tag. False negative results due to products that would inhibit the PCR reaction had been ruled out by the neat/spike technique. Our results do not support a role for polyomaviruses in the etiology of childhood brain tumors and adrenocortical carcinomas. Absence of polyomavirus DNA in our samples might be explained by the lack of participation of these viruses in the development of these particular tumors, or by the "hit-and-run" theory described by other authors.