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LETTER TO THE EDITOR

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Re: Detection of JC virus sequences in colorectal cancers in Japan

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To the Editors:

We read "Detection of JC virus DNA sequences in colorectal cancers in Japan" by Hori et al. with great excitement. These authors offer convincing evidence that polyoma T antigen may be integrated into the cellular genome of colon carcinoma tissues, although the T-antigen protein is not expressed [4]. We enthusiastically agree with their conclusions and would like to offer additional data to advance this discussion.

First, we have investigated the presence of polyomavirus (PV) T antigen in tumors by immunohistochemistry (IHC), using a primary antibody that reacts with the large T antigen of both the JC and BK viruses [1, 5]. T antigen was not detected in any of 50 cases of colon carcinoma, 18 cases of gastric cancer, or 15 cases of bladder carcinoma.

In addition, we examined by IHC the presence of T antigen in six cases of polyoma virus nephropathy (PVN) in renal transplant patients. In all of these six patients, robust nuclear staining specific for T antigen was observed in scattered tubular cells. The infected tubular cells were characterized by distinct cytopathological features, including anisonucleosis, hyperchromasia with clumped chromatin, and intranuclear inclusions. Such cellular changes represent a "permissive" infection, i.e., a state of viral replication. These histopathological features are absent in our 83 cases of carcinoma.

We agree with these authors that if PV is present in tumors, it is likely to be integrated into the cellular genome, representing a "nonpermissive" infection in which viral replication does not occur.

We conclude that future IHC studies of tumors are likely to be uninformative because we fail to detect viral antigens in nonpermissive infections, which are precisely the category of infections hypothesized to drive oncogenesis. Although recent studies have detected T antigen by IHC in esophageal [2] and colon [3] carcinoma, it remains to be seen whether these data truly represent evidence for a viral etiology in these tumors, or, alternatively, a sequelae of the patient's immunocompromised state.

We look forward to hearing the results of future studies from Dr. Hori's team.

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