

**Formation of Brain Tumor and Lymphoma by Deregulation of Apoptosis
Related Gene Expression in VP-SV40 T Ag Transgenic Mice**

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The neuropeptide vasopressin (VP) is a nine- amino acid hormone synthesized as preprohormone in the cell bodies of hypothalamic magnocellular neurons. The tumor in magnocellular neurons of the hypothalamus is associated with disfunctions of the cell bodies, leading to the diabetes insipidus. In order to study with the diabetes insipidus caused by a defect in VP synthesis and its secretion, we have produced the transgenic mice regulated by vasopressin promoter inserted to SV40 T antigen coding sequence (pVPSV.IGR2.1). One transgenic line expressing high levels of SV40 T antigen was propagated. The founder and all transgene positive adult animals have appeared with shorten mortality or apparent phenotypic abnormalities, including immune complex disease, and eventually die between 4 and 8 months of age. The mRNA and protein of SV40T antigen transgene were detected in brain of fetus as well as in brain, spleen, lung and lymph node in moribund at the age of 20 weeks. Histological analysis of transgenic mice showed that tumor developed in brain similar to primitive neuroectodermal tumors (PNET) in man. We also detected lymphomas in spleen and lymph node, and consequent tumor formation in various tissues of the transgenic mice. In pVPSV.IGR2.1, 21% mice showed brain tumor (PNET) at 5 weeks and 100% mice showed brain tumor after 15 weeks. In addition, Expression of apoptosis related genes (Bcl-2 & Bax) was increased over their age in mice with PNET as compared to control mice. Apoptosis related gene expression might be deregulated in mice with brain tumor. However, transgenic mice were not developed with the diabetes insipidus. These mice represent the first disease model to exhibit primitive neuroectodermal tumor in brain, as well as a unique model system for exploring the cellular pathogenesis of lymphomas.

(Key words) **VP, SV40T antigen, Diabetes Insipidus, PNET.**