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Tumorigenesis of Transgenic Mice Induced by Mouse Vasopressin-SV40 T Hybrid Oncogene

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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 produce the disease models with a defect in VP synthesis and its secretion, we have produced the transgenic mice regulated by VP constructs containing 3.8 kbp of the 5'flanking region and all the exons and introns in the mouse VP gene, which was fused at the end of exon 3 to a SV40 Tag. The two VP-transgene constructs differed by the lengths of their VP gene 3' flanking regions (2.1 versus 3.6 kbp). In pVPSVIGR3.6 construct, all six of founder transgenic mice were died the age of 2-4 weeks, and among three transgenic mice in pVPSVIGR2.1 construct. One transgenic line expressing high levels of SV40 T antigenwas propagated. The founder and all transgene positive adult animals have appeared with shorten mortality or apparent phenotypic abnormalities, including immune complex disease, and 21% mice showed brain tumor at 5 weeks and 100% mice showed brain tumor after 15 weeks.

Histological analysis of transgenic mice showed that tumor developed in brain is similar to primitive neuroectodermal tumors (PNET) in man and tumor in immune tissue is similar to lymphoma in man. In addition, the expression of apoptosis related genes (Bcl-2 & Bax) was increased over their age and might be deregulated in mice with PNET.Therefore, these expression vectors regulate differently in the transgenic mice and suggested that the tissue-specific expression might be regulated by cis-acting elements in 1.5 kbp 3'flanking region without the pVPSVIGR2.1 construct. However, these mice represent the first disease model to co-exhibit both non-matastastic tumor in brain and matastastic tumor in lymph node, and a unique model system for exploring the cellular pathogenesis of tumors.

key words) ***vasopressin, SV40, transgenic mice***