

Gene analysis of Epstein-Barr virus-associated lymphomas in Hu-PBL/SCID chimeras

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ABSTRACT

Aims and background. The mechanisms of Epstein-Barr virus (EBV)-associated tumor development are incompletely understood. The aim of this study was to investigate the gene expression of EBV-associated lymphomas in hu-PBL/SCID mice.

Methods. Human peripheral blood lymphocytes (hu-PBL) from EBV-seropositive donors were transplanted into severe combined immunodeficiency (SCID) mice. *In situ* hybridization was used to detect EBV-encoded small RNA-1 (EBER1) in tumor tissues. Mutation of *TP53* exons 5-8 in EBV-induced lymphomas was analyzed by PCR-SSCP. Immunohistochemical staining was used to examine EBV gene products and cellular oncoproteins.

Results. Twenty-one of 29 mice developed tumors. EBER1 was positive in the nuclei of almost all tumor cells. Immunohistochemistry showed positive staining of LMP1, EBNA2 and ZEBRA in a small number of tumor cells. Immunohistochemically detectable p53 protein expression was common (85.7%), but *TP53* gene mutations were identified in only four cases (19.1%) of EBV-associated lymphomas. Positivity rates of C-myc, Bcl-2 and Bax expression were 100%, 95.2%, and 90.5%, respectively, in the 21 cases of EBV-associated lymphomas.

Conclusions. Our preliminary findings suggest that EBV-associated lymphomas in hu-PBL/SCID chimeras show EBV infection, expression of oncogenic viral genes, and overexpression of cellular oncogenes. *TP53* gene mutations are rare but p53 protein is commonly expressed in EBV-associated lymphomas. Free full text available at www.tumorionline.it

Key words: Epstein-Barr virus (EBV), induced lymphoma, oncogenes, *TP53*, hu-PBL/SCID chimera

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