Expression of Cell-Homologous Genes of Human Herpesvirus-8 in Human Immunodeficiency Virus-Negative Lymphoproliferative Diseases

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Human herpesvirus-8 (HHV-8) genome encodes for genes homologous to human cellular genes such as interleukin-6 (IL-6), Cyclin-D, BCL-2, and IL-8 receptor (G-protein-coupled receptor [GCR]). We used reverse transcriptase-polymerase chain reaction to study the expression of these viral genes in lymphoproliferative disorders associated with HHV-8 infection. None of these genes was expressed in 1 case of benign, localized Castleman’s disease (CD), and only viral IL-6 and viral Cyclin-D were transcribed in 2 cases of benign lymphadenopathies with giant germinal center hyperplasia and increased vascularity. In contrast, all 4 genes were transcribed in 1 case of multicentric CD of plasma cell type with aggressive clinical course and in 1 primary effusion lymphoma cell line. Our study provides the evidence that various HHV-8 genes, homologous to cellular genes involved in control of proliferation and apoptosis, may be differentially expressed in different lymphoid disorders in vivo.

RESULTS AND DISCUSSION

The results of the expression studies are summarized in Table 1 and in Fig 1. Expression of all 4 HHV-8 transcripts was undetectable in the HHV-8 DNA-negative samples (not shown; Fig 1).

Our study reports, for the first time, that (1) HHV-8 genes, homologous to cell genes, may be transcribed in lymphoid tissues in vivo, out of the KS and acquired immunodeficiency syndrome (AIDS) settings; (2) the expression of such viral genes is apparently different in the different lymphoproliferative diseases of our series, associated with HHV-8 infection, namely in benign (reactive lymphadenopathy and localized CD
of HV type), atypical (multicentric CD [MCD] of PC type), and malignant (PEL) lymphoproliferative diseases. Our findings, although obtained on these few, rare cases, also suggest that the pattern of expression of HHV-8 genes homologous to cellular genes involved in cell proliferation (v-cyclin-D and vGCR) and apoptosis (vIL-6 and vBCL-2) may influence the nature of the lymphoproliferative process associated with this herpesviral infection.

Consistent with the transcription mapping of HHV-8 genome in the BC-1 lymphoma cell line using Northern blot analysis, our study may also suggest that, in the 2 cases of benign lymphadenopathies, the expression of v-cyclin-D and vIL-6 reflects a predominantly latent HHV-8 infection. Conversely, the expression of vGCR, documented in the case of MCD of PC type as well as in the HBL-6 cell line, suggests that HHV-8 is likely to replicate there, at least in a proportion of infected cells.

Expression studies on a larger series of different lymphoproliferative diseases are necessary to understand if the differential expression of some HHV-8 genes is one of the possible mechanisms of HHV-8–induced lymphoproliferation in vivo.5,7

REFERENCES


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