BRIEF REPORT

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

By Mario Luppi, Patrizia Barozzi, Antonio Maiorana, Raffaella Trovato, Roberto Marasca, Monica Morselli, Katia Cagossi, and Giuseppe Torelli

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 lymphoproliferative disorders 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. © 1999 by The American Society of Hematology.

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,11 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

### Table 1. Expression Studies of Cell-Homologous Genes of HHV-8 by RT-PCR in Lymphoproliferative Diseases

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>vIL-6</th>
<th>v-Cyclin-D</th>
<th>vBCL-2</th>
<th>vGCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoid tissues</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reactive lymphadenopathy</td>
<td>Pos</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>Reactive lymphadenopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD (multicentric, PC type)</td>
<td>Pos</td>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>CD (localized, HV type)</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>PEL cell line</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBL-6</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
</tr>
</tbody>
</table>

Fig 1. (A through D) Detection by RT-PCR of the expression of cell-homologous genes of HHV-8 in 2 cases of reactive lymphadenopathy (lanes 1 and 2), in 1 case of localized CD of HV type (lane 3), in 1 case of multicentric CD of PC type (lane 4), and in 1 PEL cell line (HBL-6). NC, Raji cell line DNA. Negative controls included RT-PCR performed on RNA in the absence of reverse transcription reaction (−). nt, nucleotides; phiX174 HaeIII digested as molecular marker.

### REFERENCES


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