Herpesvirus-Like Nucleic Acid Sequences in Patients with Eastern European Sporadic Kaposi’s Sarcoma

To the Editor:
Recent studies have shown the presence of a new γ-herpesvirus-like DNA sequence (KSHV) in different forms of Kaposi’s sarcoma (KS) [1-4]. The nucleic acid alterations observed in some classic, African endemic, and AIDS-associated specimens indicate polymorphism of the herpesvirus-like DNA [3,4]. Since epidemiologic evidence indicates that sporadic KS occurs more frequently in eastern European countries, we were interested in whether the same herpesvirus-like nucleic acid sequence is present in skin tumours of patients with sporadic KS in eastern Europe.

DNA were obtained by proteinase K digestion from 5-μm sections of formalin-fixed, paraffin-embedded tissue specimens of 24 eastern European patients with classic KS, three patients with basalioma, three patients with pyogenic granuloma, and five patients with hemangioma. All patients were HIV-negative and had not received any immunosuppressive therapy. The DNA was next analyzed for the presence of KSHV by polymerase chain reaction (PCR), using primers specific for this herpesvirus, which amplifies a 233-bp sequence designated the KS330Bam fragment, as described by Chang et al [1]. The PCR products were then analyzed on 1.5% agarose/ethidium bromide gel. All KS specimens were positive for the KS330Bam fragment, whereas these PCR products could not be generated from the other types of skin tumors, providing strong evidence of the specific association of KSHV with classic KS. Four PCR products from KS specimens were cloned into pKS, then direct sequenced by dideoxy sequencing. The sequence analysis revealed nucleic acid changes in each cloned KS330Bam fragment resulting in alterations in the amino acid sequence of the protein encoded by the KS-associated DNA open reading frame (Table I). Each sequence differed from the prototypic sequence originally derived from a genomic library made from a KS lesion [1] at a single base-pair position (1033) coding for a proline-to-leucine substitution. Since the same nucleic acid substitution at position 1033 was recently found in all three forms of KS by Moore and Chang [4], it appears that this sequence is more conservative than the prototypic sequence. PCR products from lesions in one patient (Sample 3) had an additional base-pair substitution at position 1173, coding for a tryptophan-to-isoleucine change, whereas in one patient (Sample 4) there was an additional base-pair substitution at position 1168, coding for a valine-to-methionine substitution. The significance of the sequence variations of KSHV needs to be elucidated.

The highly specific association of KSHV sequences with classic KS in the large series of patients reported here supports the concept that this virus is involved in the pathogenesis of this tumor. The KSHV sequences we found in classic KS were nearly the same as the sequence published for AIDS-associated KS, suggesting that the different forms of Kaposi’s sarcoma are probably not due to sequence variations of the KSHV. Previously we detected immune deficiencies in patients with classic KS [5]. We presume that the different clinical forms of Kaposi’s sarcoma might be due to differences in the host immune protection. The importance of the immune system in KSHV infection was further strengthened recently by the results of Rady et al [6], who detected KSHV DNA sequences in non-KS skin tumours of transplant patients, suggesting that KSHV is a widespread latent virus activated by immunosuppressive conditions. It cannot be excluded, however, that this new herpesvirus is a common virus in humans, that preferentially colonizes KS lesions in immunocompromised patients. Further investigations are necessary to establish the exact role of KSHV in the pathogenesis of KS.

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REFERENCES

Table I. Polymorphism of the Herpesvirus-Like DNA in Eastern European Kaposi’s Sarcoma

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Nucleic Acid Variations</th>
<th>Amino Acid Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C → T (1033)</td>
<td>Pro → Leu (134)</td>
</tr>
<tr>
<td>2</td>
<td>C → T (1033)</td>
<td>Pro → Leu (134)</td>
</tr>
<tr>
<td>3</td>
<td>C → T (1033)</td>
<td>Pro → Leu (134)</td>
</tr>
<tr>
<td>4</td>
<td>C → T (1173)</td>
<td>Thr → Ile (181)</td>
</tr>
</tbody>
</table>

- The numbers in brackets indicate the positions of detected nucleic acid (C) or amino acid (Pro) changes compared with the herpesvirus-like sequences originally described by Chang et al [1].

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