Lymphomas occurring in individuals infected with the human immunodeficiency virus type 1 (HIV-1) are predominantly of B-cell origin. To the Editor:

Lymphomas occurring in individuals infected with the human immunodeficiency virus type 1 (HIV-1) are predominantly of B-cell origin. We immunohistochemically stained tumors of B-cell origin not occurring in HIV-1-infected individuals similarly expressed shared idiotypes. We immunohistochemically stained 25 separate AIDS-associated B-cell lymphomas with a panel of anti-idiotypes (generous gift of Rich Miller, IDEC Pharmaceuticals, Mountain View, CA); the S2.33 idotype reacted with 7 (28%) (ie, of 178 (6.2%) cases of non-acquired immunodeficiency syndrome (AIDS) B-cell lymphomas. We were interested in determining if B-cell lymphomas occurring in HIV-1-infected individuals similarly expressed shared idiotypes. We immunohistochemically stained 25 separate AIDS-associated B-cell lymphomas with a panel of anti-idiotypes (generous gift of Rich Miller, IDEC Pharmaceuticals, Mountain View, CA); the S2.33 idotype reacted with 7 (28%) (ie, of 178 (6.2%) cases of non-acquired immunodeficiency syndrome (AIDS) B-cell lymphomas. We were interested in determining if B-cell lymphomas occurring in HIV-1-infected individuals similarly expressed shared idiotypes.
CORRESPONDENCE

and 2 of 2 low-grade lymphomas (1 CLL and 1 follicular lymphoma), and reacted with 20% to 60% of lymphocytes present in 4 of 6 lymph nodes obtained from HIV-1-infected individuals and exhibiting follicular hyperplasia.

Analysis of shared idiotypes on human B-cell tumors with well-characterized monoclonal antibodies (MoAbs) that recognize specific Ig heavy- or light-chain determinants (eg, MoAb 17.109 recognition of the κ chain variable gene humk325, MoAb 6B6.6 recognition of VκIIIα, MoAb G6 recognition of a Vλ 1 gene, and MoAb (9G4 recognition of Vκ4.21) has suggested that the observation of shared idiotypes might in fact be a phenotypic marker for expression of specific V genes. The molecular nature of the S2.33 shared idiotype is not known; the observation that S2.33 reactive lymphomas expressed either κ or λ light chains suggested to us that the S2.33 idiotope might be unique to the coexpressed Vκ gene.

An autoreactive IgM κ produced by one previously described well-characterized cell line, 10C9, derived from an AIDS-associated Burkitt's lymphoma, was S2.33 reactive and used a Vκ 4 gene 95% related to the Vκ 4.21 gene. Preferential use of the Vκ 4.21 gene has been shown with antibodies associated with autoimmune disease; the relatively high frequency of S2.33 binding to human B-cell lymphomas suggested that the S2.33 anti-idiotype might be a marker for use of the Vκ 4.21 gene. To pursue this hypothesis, we determined the Vκ gene used by the leukemic cells of an S2.33-reactive AIDS-associated CLL (BR). The Vκ gene was amplified using the polymerase chain reaction (PCR) from DNA extracted from paraffin-embedded tissue and previously described methods. A single PCR product was observed with a 5' Vκ 3 leader sequence/3' consensus Jκ primer pair. Nucleotide sequence showed the PCR product to be 100% homologous to a previously described germline Vκ 3 gene, 22-2B. The Vκ gene used by BR was not determined. When the two nucleotide sequences (Fig 1A) or predicted amino acid sequences (Fig 1B) of the 10C9 and BR Vκ genes were aligned, there were no obvious regions of homology to serve as candidates for a shared idiotope. An idiotope could theoretically be as small as 5 amino acids; the only linear stretches of the 2 Vκ genes to satisfy that requirement were between codons 43 through 47 and 86 through 94, the sequences of which were identical to that of another IgM produced by an AIDS lymphoma cell line, 2F7, which failed to react with S2.33. The possibility that the Vκ 4 antigen binding hypervariable region (ie, H1 and H2 canonical structures that are adjacent to and slightly overlap the complementarity determining regions) constituted the idiotope was considered when BR and 10C9 were observed to have the same type 1 H1 canonical structure; however, this possibility was eliminated when the 2F7 IgM was also noted to have the same type 1 H1 canonical structure.

In contrast to other studies that have used well-characterized MoAbs to show "shared idiotypes," we present preliminary evidence that the S2.33 anti-idiotype recognizes a shared idiotype encoded by at least two different Vκ gene families (ie, Vκ 3 and Vκ 4). The molecular nature of the idiotope remains unknown, but may be an as-yet-unidentified secondary or tertiary structure common to both Vκ genes, or a structural determinant contributed by both the Vκ and Vλ genes.

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REFERENCES

Inter-VH-gene-family shared idiotype on acquired immunodeficiency syndrome-associated lymphomas [letter]

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