Further Evidence for In Vivo Isotype Switching in B-Cell Chronic Lymphocytic Leukemia

To the Editor:

In a recent article in Blood, Malison et al have reported experimental evidence in support of in vivo isotype switching in B-cell chronic lymphocytic leukemia (CLL). The evidence was that freshly isolated sIgM⁺ sIgG⁻ sIgA⁻ B-CLL cells nevertheless express IgG and IgA transcripts that have identical VDJ segments and that these cells may be induced in vivo to secrete IgG and IgA. Based on our own published observations, we most definitely agree with this conclusion.

We have described an unusual case of small lymphocytic lymphoma/CLL in which the small B lymphocytes were sIgM⁺ sIgA⁻ K⁺, whereas the larger B prolymphocytes within the proliferation centers were sIgM⁻ sIgA⁺ K⁺. Southern blot DNA analysis showed that there were 2 J₅ rearrangements (1 that cohybridized with a C₅ probe and 1 that cohybridized with a C₆ probe), whereas there was but a single C₅ rearrangement. These data therefore indicated that the larger IgA⁺ prolymphocytes arose from the small IgM⁺ lymphocytes by an in vivo heavy chain isotype switch.

The idea proposed by Malison et al that the translation blockade of the CLL cells is due to a deficient microenvironment is very intriguing. In our case, the fully switched cells were larger prolymphocytes that congregated in proliferation centers. The proliferation center of CLL vaguely resembles a germinal center yet is deficient in cells that may be important in promoting complete isotype switching, i.e., follicular dendritic cells and T cells. Indeed, in our case, the rare T cells that were present were admixed with the diffuse small lymphocytic infiltrate while sparing the proliferation centers. As suggested by Malison et al., in some cases other signals, e.g., autoantigen, may provide the necessary signals for isotype switching.

Thus, although full translation of isotype-switched Ig in CLL cells is only rarely identified in vivo, it may be that under some unusual circumstances the signals are generated within germinal center-like proliferation centers.

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REFERENCES


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