With regard to the differences in the minimal residual disease criteria and for a CR between the published and online versions, we wish to emphasize that due to a series of unfortunate events, the version published in paper form in June 2008 was not approved by the authors. Only the final version of the manuscript published in December 2008 was approved by the authors of the paper.

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References


To the editor: MALT lymphoma–derived rheumatoid factors are nonpolyreactive high-affinity antibodies

We have read with particular interest the paper of Craig et al., describing that 6 of 7 human mucosa-associated lymphoid tissue (MALT) lymphoma–derived immunoglobulins (Igs) bound various antigens with intermediate affinity, thus implying that MALT lymphomas express polyreactive antigen receptors. We previously reported that MALT lymphomas frequently express Igs, which are homologous to canonical rheumatoid factors (RFs), encoded by unmutated V1-69 RFs, which are reported to be polyreactive and nonpolyreactive.

Prompted by the results by Craig et al., we tested the binding characteristics of 7 of our MALT lymphoma Igs, 4 of which were homologous to canonical RFs (ie, M5, M6, M11, and M22) in ELISAs. This study was conducted in accordance with the Declaration of Helsinki and the ethical standards of the research code committee on human experimentation of the Academic Medical Center of Amsterdam. As controls, we included 2 IgVH-mutated and 2 IgVH-unmutated B-cell chronic lymphocytic leukemia (CLL)–derived Igs, which are reported to be polyreactive and nonpolyreactive, respectively. In contrast to the data presented by Craig et al., 6 of 7 MALT lymphoma Igs, including the 4 RFs, reacted only with IgG or were nonreactive (Figure 1A), as may be expected from somatically mutated Igs. Only MALT lymphoma Ig M23 did bind several antigens. As expected, the 2 mutated CLls were nonreactive whereas the 2 unmutated CLls bound to essentially all antigens tested. In general, the M23 Ig showed a lower degree of polyreactivity compared with the unmutated CLL–derived Igs.

To further explore the reactivity of the MALT lymphoma Igs, we used the recombinant Igs in immunohistochemical stainings of tissue microarrays (TMAs) containing 21 paraffin-embedded normal human tissues. None of the MALT lymphoma Igs reacted with any of the tissues on the TMA, except for M23, which showed broad reactivity (Figure 1B). Similarly, the unmutated CLL Igs stained all the tissues tested, even at low concentrations. It is noted that the polyreactive MALT lymphoma M23 differs from the other MALT lymphomas in that it harbors a t(11;18)(API-MALT). This chromosomal translocation results in the constitutive activation of the nuclear factor kB (NF-kB) pathway, potentially rendering the cells independent of antigen receptor signals and thus disturbing the process of antigenic selection.

Our finding that MALT lymphoma RFs are monoreactive, is concordant with several papers in which V1-69/Vk3-20 RFs are compared with unmutated V1-69–encoded CLL Igs, demonstrating that mutated V1-69/Vk3-20 RFs are nonpolyreactive, whereas unmutated V1-69 CLl Igs show low-affinity binding to multiple antigens, including IgG.
We conclude that V1-69/Vk3-20 and V3-7/Vk3-15 MALT lymphoma–derived Igs are ligand-selected, monospecific high-affinity antibodies.

**References**


**Response**

Gastric MALT lymphoma–derived tumor immunoglobulins are polyreactive and respond to a variety of self and foreign antigens.

Multiple attempts have been made in the past 2 decades to delineate the antigen specificity of tumor immunoglobulins expressed by mucosa-associated lymphoid tissue (MALT) lymphoma. These studies have produced rather discrepant results, which may be attributable to the different approaches to tumor-derived antibody generation and their screening. The tumor Ig specificity further...
MALT lymphoma–derived rheumatoid factors are nonpolyreactive high-affinity antibodies

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