Regulatory B Cells Inhibit Antitumor Immunity

In Response:

Depleting B cells as part of a tumor-therapy regimen is an idea that becomes increasingly attractive as more studies show an apparent inhibitory role of host B cells on antitumor immune responses. However, it seems that Shah et al. (1) and our results (2) suggest different mechanisms responsible for the suppression of antitumor immunity by B cells. Our own study had been designed to investigate the regulatory role of B cells in antitumor immunity. B cells including regulatory B cells (B<sub>reg</sub> cells) exist in large numbers in the marginal zone of the mouse spleen (3). Therefore, we had isolated B cells from mouse spleen using a monoclonal antibody specific for the commonly used B cell marker CD19. Our data clearly showed that interleukin-10 (IL-10) produced by B<sub>reg</sub> cells reduced the IFN-γ production from CTL and natural killer cells partially in a CD40-CD154–dependent manner in vitro (2). In contrast, Shah et al. suggested that the inhibitory effect of B cells on tumor rejection may not be associated with CD40 expression on B cells due to the inconsistent results between in vitro and in vivo studies (1). Why do these results seem to be conflicting with our findings? We believe that the answer can be found in experimental details of these studies. Shah et al. purified B cells from mouse spleen by negative selection using anti-CD43 antibody, which is frequently used for B cell enrichment because this molecule is not expressed on conventional B cells (3). However, CD43 may be expressed on B<sub>reg</sub> cells (4) and, thus, such regulatory B cells may have been excluded from their experiments.

In our experiments, we used neither CD40-CD154–inhibiting antibody nor CD40-deficient B cells for in vivo experiments to avoid experimental artifacts due to the critical role the binding of CD40 to CD154 plays outside the predicted B cell-tumor cell interaction. Based on our studies, we do believe that the interaction between CD40 on B<sub>reg</sub> cells and CD154 on tumor cells is associated with the mechanism by which antitumor immunity is enhanced in the absence of B cells. Whatever the precise mechanism may be, we agree that B cell depletion by rituximab could provide beneficial effects on cancer immunotherapy (1, 2), although the specific depletion of B<sub>reg</sub> cells may be the more promising and more desirable approach.

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References

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