T-Cell Response in B-Cell Lymphomas: Favorable or Unfavorable?

To the Editors: In a recent issue of Clinical Cancer Research, Chang and colleagues reported that in patients with diffuse large B-cell lymphoma, the presence of an intense cytotoxic T-cell infiltrate was associated with a favorable clinical outcome (1). These observations are in contrast with our previous reports, and by other reports, which show that the presence of many activated cytotoxic T-cells in primary nodal diffuse large B-cell lymphomas is in fact a strong International Prognostic Index–independent indicator for an unfavorable clinical outcome (2, 3). We recently confirmed this association by microarray expression analysis, which also identified a group of patients with primary nodal diffuse large B-cell lymphoma with a very poor clinical outcome that was characterized by high expression levels of cytotoxic T-cell effector molecules including granzyme B and perforin (4). The possible causes for these conflicting data are not clear but could result from differences in the methods used for quantification of the T cells or by selection of analyzed areas of tumor specimens.

It is unclear why Chang et al. did not cite these previous articles. Chang et al. conclude that enhancing this putative antitumor T-cell immune response is a possible target for diffuse large B-cell lymphoma immunotherapy (1). Based on our data, and the data reported by Hasselblom et al. (3), we think that this is unlikely. Apparently, in cases with many activated CTLs, these T cells are also incapable of effectively killing the lymphoma cells. Hasselblom et al. showed that this is probably not caused by the presence of Foxp3 immunosuppressive T cells (3). We have previously suggested that lymphoma cells might escape from CTL-induced apoptosis not only by interfering with proper antigen presentation but also by disruption of the intracellular apoptosis pathway (2). This latter mechanism could also explain the poor response to the apoptosis-inducing chemotherapy. Thus, from this point of view, not enhancing the antilymphoma T-cell response, but rather, restoring apoptosis sensitivity will be a promising new therapy for patients with chemotherapy-refractory diffuse large B-cell lymphoma. Recently, we have shown that this is indeed a highly promising approach (5).

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References
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