Chapter 8

CD22 is not expressed merely on B-cells

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A recent report on the early depleting effects of rituximab in the synovial tissue of patients with rheumatoid arthritis (RA) showed that the tissue depletion of CD22+ cells was incomplete. Recently, our group reported the depleting effects of rituximab in paired samples of peripheral blood, bone marrow, and synovium. The latter study revealed a complete depletion of the CD20+ subset of B-cells in synovium, as shown by staining the cytoplasmic tail of the CD20 membrane protein. Our results and those of Vos et al. are seemingly contradictory, and the existence of a CD22+, CD20- B-cell subset may be relevant to the pathogenic mechanisms of RA. Therefore, we investigated the specificity and sensitivity of CD22, CD19, and CD20 as markers of B-cells.

Briefly, peripheral blood mononuclear cells from 5 healthy volunteers were obtained through isolation over a Ficoll gradient and freshly stained with the following markers: fluorescein isothiocyanate (FITC)-conjugated anti-CD20 (clone 2H7); phycoerythrin-conjugated anti-CD19 (clone H1B19); allophyco-cyanin (APC)-conjugated anti-CD22 (clone S-HCL-1); APC-conjugated anti-CD3 (UCHT1); and FITC-conjugated anti-CD3 (clone 5K7) (all from BD Biosciences, San Jose, CA). After incubation for 30 minutes in the dark, cells were washed and read on a FACSCalibur flow cytometer (BD Biosciences) and analyzed with FlowJo software program (Tree Star, Ashland, OR). We observed that 97.6% of CD19+ cells and 96.7% of CD20+ cells were CD22 positive. However, only 78.1% and 75.2% of CD22+ cells were positive for CD19 and CD20, respectively (P=0.04, by Mann-Whitney-U test) (Table 1).

<table>
<thead>
<tr>
<th>Gated population</th>
<th>CD22</th>
<th>CD19</th>
<th>CD20</th>
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</thead>
<tbody>
<tr>
<td>CD22+ cells</td>
<td>100</td>
<td>78.1</td>
<td>75.2</td>
</tr>
<tr>
<td>CD19+ cells</td>
<td>97.6</td>
<td>100</td>
<td>96.7</td>
</tr>
<tr>
<td>CD20+ cells</td>
<td>99.3</td>
<td>99.0</td>
<td>100</td>
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</tbody>
</table>

Table 1 Expression of CD2, CD19, and CD20
In conclusion, these data indicated that CD22 is not a specific marker for B-cells, raising the possibility that in the study by Vos et al. the residual CD22 positivity after rituximab treatment can be explained by the presence of cell types not belonging to the B-cell lineage. In this context, Han et al. previously reported that in healthy persons basophils can be isolated with a purity of 99.4% by sorting CD22+, CD19- lymphocytes. Mast cells (tissue-infiltrating basophils) do not seem to express CD22 on their membrane but do show intracellular messenger RNA expression of CD22. Therefore, we believe further research into the residual CD22-expressing cells is warranted, and that the results of CD22 single-staining should be interpreted with caution when used in the context of B-cell depletion with rituximab.
References


