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# Structural Relatedness of Distinct Determinants Recognized by Monoclonal Antibody TP25.99 on ß$_2$-Microglobulin-Associated and ß$_2$-Microglobulin-Free HLA Class I Heavy Chains

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The association of HLA class I heavy chains with ß$_2$-microglobulin (ß$_2$m) changes their antigenic profile. As a result, Abs react with either ß$_2$m-free or ß$_2$m-associated HLA class I heavy chains. An exception to this rule is the mAb TP25.99, which reacts with both ß$_2$m-associated and ß$_2$m-free HLA class I heavy chains. The reactivity with ß$_2$m-associated HLA class I heavy chains is mediated by a conformational determinant expressed on all HLA-A, -B, and -C Ags. This determinant has been mapped to amino acid residues 194–198 in the $\alpha$3 domain. The reactivity with ß$_2$m-free HLA class I heavy chains is mediated by a linear determinant expressed on all HLA-B Ags except the HLA-B73 allospecificity and on <50% of HLA-A allospecificities. The latter determinant has been mapped to amino acid residues 239–242, 245, and 246 in the $\alpha$3 domain. The conformational and the linear determinants share several structural features, but have no homology in their amino acid sequence. mAb TP25.99 represents the first example of a mAb recognizing two distinct and spatially distant determinants on a protein. The structural homology of a linear and a conformational determinant on an antigenic entity provides a molecular mechanism for the sharing of specificity by B and TCRs.

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