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# Structural Relatedness of Distinct Determinants Recognized by Monoclonal Antibody TP25.99 on $\beta_2$ -Microglobulin-Associated and $\beta_2$ -Microglobulin-Free HLA Class I Heavy Chains

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## **Structural Relatedness of Distinct Determinants Recognized by Monoclonal Antibody TP25.99 on $\beta_2$ -Microglobulin-Associated and $\beta_2$ -Microglobulin-Free HLA Class I Heavy Chains**

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The association of HLA class I heavy chains with  $\beta_2$ -microglobulin ( $\beta_2m$ ) changes their antigenic profile. As a result, Abs react with either  $\beta_2m$ -free or  $\beta_2m$ -associated HLA class I heavy chains. An exception to this rule is the mAb TP25.99, which reacts with both  $\beta_2m$ -associated and  $\beta_2m$ -free HLA class I heavy chains. The reactivity with  $\beta_2m$ -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  $\beta_2m$ -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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