Analysis of functional sites on a peptide antigen, p43–58, in IA or IE-restricted T cell responses

Abstract:

It has been shown that two different sites (an agretope and an epitope) on a peptide antigen function independently In T cell responses to the antigen. By virtue of these sites, antigens, MHC molecules, and TCRs constitute trimolecule complexes which eventually result In T cell activation. In our previous reports, we have defined that residues 46 and 54 on a synthetic peptide composed of residues 43–58 of pigeon cytochrome c (p43–58, AEGFSYTDANKNKGIT) and its analogs function as an agretope and residue 50 as an epitope In both I-Ab and I-Ak-carrying mice. In the present study, to extend our method to the other MHC class II molecules (I-E), we used two peptide antigens, 46D50V54R and 50V54R, which had been prepared by substitution of amino acids at positions, 46, 50 and 54 or 50 and 54 of p43 – 58 with D, V, R or V, R, respectively, and compared the Immunogeniclty with those of other peptide analogs. The 46D50V54R was shown to be non-immunogenic In I-Ab-carrylng mice and the 50V54R was non-Immunogenlc in l-Ak-carrylng mice. In contrast, the 46D50V54R or 50V54R could Induce I-E-restrlcted proliferatlve responses of T lymphocytes In I-Eb/k- or I-Ek/k-carrylng mice, respectively. Furthermore, residues 46 and 54 were shown to function as agretopes and residue 50 as an epitope In the l-E-restrlcted responses as they did In the l-A-restrlcted responses, even though some differences were seen between peptide-I-E Interaction and peptide -I-A Interaction. These agretopes and epitope functioned independently.