he T Cell Responsiveness To Synthetic Peptides By Substituting Amino Acids On Agretopes.

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Abstract:

T cell receptors, major histocompatibility complex molecules, and antigens constitute tri-molecular complexes which induce T cell activation. T cells in I-Ab mice generate proliferative responses to a synthetic peptide composed of residues 43-58 of pigeon cytochrome c (p43-58) and its analogs with substitution at position 50 (50A, 50V, 50L, 50N, 50Q, 50K, and 50M). However, none of these peptides stimulate T cells in I-Ak mice. We substituted two residues at positions 46 and 54 of p43-58(50D), 50V, 50L, 50E, and 50K with two amino acids on agretopes of the I-Ak binding HEL52-61 peptide and immunized I-Ak mice with these newly synthesized peptides: 46D50D54R, 46D50V54R, 46D50L54R, 46D50E54R, and 46D50K54R. Apart from 46D50D54R, these peptides elicited T cell responses in I-Ak mice in an immunogen-specific manner, but did not stimulate those in I-Ab mice. Further, 46D50V54R inhibited competitively the responses of I-Ak restricted T cell hybridomas specific for 46D50E54R. These results demonstrate that the residues at positions 46 and 54 on the peptides act as an agretope and the residue at position 50 acts as an epitope in I-Ak mice, as in I-Ab mice, and provide the possibility of opening up a new method to prepare peptide antigens which induce T cell responses in each murine strain by introducing appropriate amino acids on agretopes