

Induction of Autoantigen-specific Th2 and Tr1 regulatory T cells and Modulation of Autoimmune Diabetes

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Autoantigen-based immunotherapy can modulate autoimmune diabetes, perhaps due to the activation of antigen specific regulatory T cells. Studies of these regulatory T cells should help us understand their roles in diabetes and aid in designing a more effective immunotherapy. We have used Class II MHC tetramers to isolate antigen-specific T cells from non-obese diabetes (NOD) mice and BALB/c mice treated with glutamic acid decarboxylase (GAD65) peptides (p206 and p221). Immunization with the same peptide induced more polarized T cell subsets in NOD mice than in BALB/c mice, based on their cytokine secretion profiles. Treatment of NOD mice induced not only IL4/IL10-secreting Th2 cells but also IFN γ /IL10-secreting Tr1 regulatory T cells. The isolated tetramer⁺ T cells specific for p206 or p221 (N206⁺ and N221⁺ cells) were able to suppress the proliferation of other NOD mouse T cells, including diabetogenic T cells, without cell-cell contact and could inhibit diabetes. They performed their regulatory function probably by secreting cytokines, and antibodies against these cytokines could block their suppressive effect. Interestingly, the presence of both anti-IL10 and anti-IFN γ could enhance the target cell proliferation, suggesting that Tr1 cells play an important role. Therefore, treatment of NOD mice with autoantigen can induce Th2 and Tr1 regulatory cells that are able to suppress the function of other T cells, including diabetogenic T cells, and inhibit diabetes development.