

Similar induction of autoimmunity by highly homologous self and foreign antigenic peptides. Abigail C. Buenafe and Lisa Watson. Department of Neurology, Oregon Health Sciences University, Portland, OR

We compared the induction of experimental autoimmune encephalomyelitis (EAE) in the Lewis rat using two homologous peptides of myelin basic protein representing self (rat MBP69-89, GSLPQKSQRTQDENPVVHF) and foreign (Gp-BP69-89, GSLPQKSQRSQDENPVVHF) antigenic peptides. Our expectation was that the self peptide would induce only a mild disease which would follow from the concept that T cells with higher affinity for self antigens are deleted during the negative selection process. Interestingly, we found that both the self and the foreign MBP peptides induced a superimposable disease course in Lewis rats with very similar severity and duration. However, proliferative analysis of lymph node and spinal cord-derived T cells indicated a better responsiveness to the foreign peptide in GpBP69-89-immunized animals and poor responsiveness to both peptides in rat MBP69-89-immunized animals. A molecular analysis of spinal cord T cells responding to either peptide indicated that different T cell populations were induced to enter the CNS - a clonotype dominant response was observed to GpBP69-89 but not to rat MBP69-89. Our current data indicate that, as a result of repertoire selection, self and foreign peptides induce different pathogenic T cell populations to respond, but that both are capable of inducing a similar disease course. We are interested in determining the affinity/avidity range associated with both responding populations to better understand the role of affinity/avidity in autoimmune disease induction.