Viruses could be involved in the induction of immunopathological events associated with multiple sclerosis (MS). For instance, molecular mimicry between viruses and myelin antigens could mediate cross-reactive immune responses leading to autoimmune disease. We previously showed that a human respiratory coronavirus (229E) and myelin basic protein (MBP) activated a large proportion of T-cell lines established from MS patients by in vitro selection with either 229E or MBP. We now report the generation and maintenance of T-cell clones specific for MBP, proteolipid protein (PLP) and the two known strains of human coronavirus (229E and OC43). Some of these clones were activated by both coronavirus and myelin antigens, which is consistent with molecular mimicry at the single T-cell level. The observation and further characterization of such T-cell clones will bring us closer to a better understanding of their potential relevance in MS pathogenesis.

Cross-reactivity with environmental antigens has been postulated as a mechanism responsible for the induction of autoimmune disease. Experimental autoimmune encephalomyelitis (EAE) is a T cell mediated autoimmune disease model inducible in susceptible strains of laboratory animals by immunization with protein components of myelin. We used myelin proteolipid protein (PLP) peptide 139-151 and its analogs to define motifs to search a protein database for structural homologues of PLP 139-151 and identified five peptides derived from microbial antigens that elicit immune responses that cross-react with this self-peptide. Exposure of naive SJL mice to the cross-reactive environmental peptides alone was insufficient to induce autoimmune disease even when animals were treated with antigen non-specific stimuli (superantigens, LPS). However, immunization of SJL mice with suboptimal doses of PLP 139-151 peptide after priming with cross-reactive environmental peptides consistently induced EAE. These data suggest that expansion by self-antigen is required to break the threshold to autoimmune disease in animals primed with cross-reactive peptides.