

BCR Peptide-directed T Cell Help During a T-dependant Immune Response Results in Abortive Germinal Center Reactions.

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An important problem in immunoregulation is how the immune system handles somatically generated antibody diversity, which is amplified during B cell clonal expansion. Some of this diversity in CDR3 predates B cell activation, while some is created de novo by the somatic hypermutation process during T cell-dependant immune reactions. Peptides derived from somatically mutated immunoglobulin genes can be presented within MHC II molecules on the surface of activated B cells and are essentially neo antigens with respect to the peripheral CD4⁺ T cell repertoire. Earlier work from our laboratory supports the hypothesis that these BCR-derived antigens can provide an avenue of T cell help to activated B cells. Our lab is interested in whether or not this mechanism plays a role in helping autoreactive B cells escape peripheral tolerance in SLE. My work utilizes a pair of transgenic mice one of which expresses a kappa light chain containing a defined T cell epitope, and another mouse that expresses a transgenic TCR capable of recognizing this epitope when presented in I-A^k. Co-adoptive transfer of these transgenic B and T cells into recipient animals allows us to recapitulate a scenario where B cells involved in an immune response to a foreign antigen interact with CD4⁺ T cells providing help to somatically generated epitopes. Preliminary results suggest that BCR-peptide specific T cell help disrupts germinal center reactions, perhaps in favor of a short-lived plasma cell response.