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Light Chain Editors and Autoimmunity

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Antibody kappa (k) genes can undergo multiple rearrangements. This is important because of the high frequencies of aberrant rearrangement and autoreactivity that are generated by rearrangement. These nonfunctional, VkJk genes or the VkJks associated with autoantibodies are nested within Vs and Js so that secondary rearrangements can replace the initial VJ gene.

This mechanism of correction - "editing"- is unique to k; neither the lambda locus nor the VH locus allows for replacement. Because editing is the major mechanism of self-tolerance, we wondered what happens to a B cell that is unable to edit. We addressed this question by studying the repertoire of B cells in mice that lack the k locus, k-/k- mice. The pre-B cells of these mice move directly to the end of the line of L chain expression, the lambda locus. The options of lambda-associated B cells other than those that were either successfully edited by one of the lambda chains. We analyzed the repertoire of lambda-associated to determine alternative mechanisms of tolerance. Both the lambda and Heavy chain loci were found to have unusual mechanisms of editing.