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B cell development and immunoglobulin genes in cattle

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Abstract

The objective of this dissertation was to study B cell development and the mechanism of immunoglobulin gene diversification in cattle. The bovine immune system differs from that of the mouse and human in several respects. First, the bovine have an unique lymphoid tissue, the ileal Peyer's patch (IPP). Secondly, at least 90% of the immunoglobulin molecules produced by bovine are of the lambda (λ) isotype.^ Northern blot and FACS analysis were performed in order to document the distribution of B cells found in calves of various ages. B cells were located in the IPP, jejunal Peyer's patch, spleen and peripheral blood. It was demonstrated that $>$90% of the IPP lymphoid cells were IgM$\sp+$ B cells. In contrast to the IPP, bone marrow of young calves did not appear to be a site for B cell development.^ To determine the mechanism by which bovine create a diverse repertoire of antibody molecules, cDNA clones encoding λ light chains from IPP B cells were sequenced. A comparison of these sequences indicated that all of the V$\sb{\lambda}$ regions were very homologous to one another, and there appeared to be three different V$\sb{\lambda}$ regions expressed. This correlated with Southern blot analyses which showed a limited number of V$\sb{\lambda}$ gene segments in the germline.^ The bovine κ light chain gene was also investigated. Based on mRNA expression and cDNA sequence analysis, it was found that cattle appear to possess a functional κ locus. Preliminary studies suggest that the bovine κ locus may have a limited number of V$\sb{\kappa}$ gene segments in the germline DNA.^ These data suggest the following: (1) IPP tissue, not bone marrow, is the major site of B cell development in a young calf. (2) Bovine B cells do not depend upon a large number of V$\sb{\lambda}$ gene segments to produce their immunoglobulin repertoire. Thus, diversity must be generated by another mechanism, perhaps somatic mutation or

gene conversion. (3) Cattle are able to transcribe the κ light chain gene, although the number of V$\sb{\kappa}$ gene segments may be limited in number. ^

Subject Area

Biology, General|Biology, Molecular

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