Structure and Function of Variable Lymphocyte Receptors: An Update

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Instead of T-cell and B-cell receptors, jawless vertebrates such as lamprey and hagfish use variable lymphocyte receptors (VLRs) as antigen receptors. VLRs generate diversity comparable to that of immunoglobulins (Ig) by assembling highly diverse leucine-rich repeat (LRR) modules. Like Igs, they exhibit allelic exclusion, with each lymphocyte expressing a unique VLR molecule. VLR monomers adopt a horseshoe-shaped structure characteristic of the LRR family, and VLR binds antigen on its concave surface. Both hagfish and lampreys have two types of VLRs named VLRA and VLRB. VLRB has a secretory form, and secreted VLRB functions as major agglutinating antibodies produced in response to antigen stimulation. On the other hand, VLRA is not secreted into the serum. Recent evidence indicates that lamprey VLRA+ and VLRB+ cells resemble T- and B-cells of jawed vertebrates, respectively, suggesting that a dual antigen receptor system analogous to that of jawed vertebrates also exists in jawless vertebrates. We recently identified a third VLR in the lamprey. This receptor, which we named VLRC, is expressed on a population of lymphocytes distinct from VLRA+ or VLRB+ cells, indicating that lampreys have three populations of lymphocytes expressing distinct VLRs.