Development of replication-defective lymphocytic choriomeningitis virus vectors for the induction of potent CD8+ T cell immunity.

Lymphocytic choriomeningitis virus (LCMV) exhibits natural tropism for dendritic cells and represents the prototypic infection that elicits protective CD8(+) T cell (cytotoxic T lymphocyte (CTL)) immunity. Here we have harnessed the immunobiology of this arenavirus for vaccine delivery. By using producer cells constitutively synthesizing the viral glycoprotein (GP), it was possible to replace the gene encoding LCMV GP with vaccine antigens to create replication-defective vaccine vectors. These rLCMV vaccines elicited CTL responses that were equivalent to or greater than those elicited by recombinant adenovirus 5 or recombinant vaccinia virus in their magnitude and cytokine profiles, and they exhibited more effective protection in several models. In contrast to recombinant adenovirus 5, rLCMV failed to elicit vector-specific antibody immunity, which facilitated re-administration of the same vector for booster vaccination. In addition, rLCMV elicited T helper type 1 CD4+ T cell responses and protective neutralizing antibodies to vaccine antigens. These features, together with low seroprevalence in humans, suggest that rLCMV may show utility as a vaccine platform against infectious diseases and cancer.