Adaptive immune responses in which CD8(+) T cells recognize pathogen-derived peptides in the context of major histocompatibility complex class I molecules play a major role in the host defense against infection with intracellular pathogens. Cells infected with intracellular bacteria such as Listeria monocytogenes, Salmonella enterica serovar Typhimurium, or Mycobacterium tuberculosis are directly lysed by cytotoxic CD8(+) T cells. For this reason, current vaccines for intracellular pathogens, such as subunit vaccines or viable bacterial vaccines, aim to generate robust cytotoxic T-cell responses. In order to investigate the capacity of a herpes simplex virus type 1 (HSV-1) vector to induce strong cytotoxic effector cell responses and protection from infection with intracellular pathogens, we developed a replication-deficient, recombinant HSV-1 (rHSV-1) vaccine. We demonstrate in side-by-side comparison with DNA vaccination that rHSV-1 vaccination induces very strong CD8(+) effector T-cell responses. While both vaccines provided protection from infection with L. monocytogenes at low, but lethal doses, only rHSV-1 vaccines could protect from higher infectious doses; HSV-1 induced potent memory cytotoxic T lymphocytes that, upon challenge by pathogens, efficiently protected the animals. Despite the
stimulation of relatively low humoral and CD4-T-cell responses, rHSV-1 vectors are strong candidates for future vaccine strategies that confer efficient protection from subsequent infection with intracellular bacteria.