Vaccine protection from CD4+ T-cell loss caused by simian immunodeficiency virus (SIV) mac251 is afforded by sequential immunization with three unrelated vaccine vectors encoding multiple SIV antigens.

Candidate human immunodeficiency virus (HIV) vaccine strategies that induce strong cellular immune responses protect rhesus macaques that are infected with recombinant simian/human immunodeficiency virus SHIV89.6p from acute CD4+ T-cell loss and delay progression to AIDS. However, similar strategies have not proven as efficacious in the simian immunodeficiency virus (SIV)mac model of AIDS, an infection that causes a slow, steady loss of CD4+ T-cell function and numbers in rhesus macaques similar to that caused by HIV-1, the principal cause of AIDS in humans. Efforts to increase vaccine efficacy by repeated boosting with the same vector are quickly limited by rising anti-vector immune responses. Here, the sequential use of three different vectors (DNA, Semliki Forest virus and modified vaccinia virus Ankara) encoding the same SIVmac structural and regulatory antigens was investigated and demonstrated to prevent or slow the loss of CD4+ T-cells after mucosal challenge with the highly pathogenic SIVmac251 strain. Of particular interest was an inverse association between the extent of T-helper 2 cytokine responses and steady-state virus load. Although limited in the number of animals, this study provides important proof of the efficacy of the triple-vector vaccine strategy against chronic,
progressive CD4+ T-cell loss in the rigorous SIVmac/rhesus macaque model of AIDS.

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