Enhanced cellular immunity and systemic control of SHIV infection by combined parenteral and mucosal administration of a DNA prime MVA boost vaccine regimen.

The immunogenicity and protective efficacy of a DNA and recombinant modified vaccinia Ankara (MVA) vaccine administered by two different routes were investigated. DNA expressing HIV-1 IIIB env, gag, RT, rev, tat and nef, and MVA expressing HIV-1 IIIB nef, tat and rev and simian immunodeficiency virus (SIV) macJ5 gag/pol and vaccinia HIV-1 env, were used as immunogens. Four cynomolgus macaques received DNA intramuscularly (i.m.) at month 0 and intrarectally (i.r.) and intra-orally (i.o.) at 2 months, followed by MVA i.m. at 4 months and i.r. and i.o. at 8 months. Another group of four monkeys received the same immunogens but only i.m. Overall, stronger cellular immune responses measured by ELISPOT and T-cell proliferation assay were detected in the group primed i.m. and boosted mucosally. Following homologous intravenous simian-human immunodeficiency virus (SHIV) challenge, one of eight vaccinated animals was completely protected. This monkey, immunized i.m. and i.r.+i.o., exhibited the highest levels of HIV Env, Nef and Tat antibodies, high HIV Tat cytotoxic T-lymphocyte activity and T-lymphocyte proliferative responses to HIV Env. Four weeks post-challenge none of the monkeys immunized i.m. and i.r.+i.o., and only
two out of four animals immunized i.m., demonstrated detectable plasma viral RNA levels. In contrast, all eight control animals had demonstrable plasma viral RNA levels 4 weeks post-challenge. Thus, stronger cellular immune responses and reduction of challenge virus burden were demonstrated in animals immunized i.m. as well as mucosally, compared with animals immunized i.m. only. The breadth and magnitude of the induced immune responses correlated with protective efficacy.