Virology

Volume 339, Issue 2, 1 September 2005, Pages 164-175

Enhanced immunogenicity and protective effect conferred by vaccination with combinations of modified vaccinia virus Ankara and licensed smallpox vaccine Dryvax in a mouse model

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https://doi.org/10.1016/j.virol.2005.06.002

Abstract

Significant adverse events are associated with vaccination with the currently licensed smallpox vaccine. Candidate new-generation smallpox vaccines such as the replication-defective modified vaccinia virus Ankara (MVA) produce very few adverse events in experimental animals and in limited human clinical trials conducted near the end of the smallpox eradication campaign. Efficacy evaluation of such new-generation vaccines will be extraordinarily complex, however, since the eradication of smallpox precludes a clinical efficacy trial and the correlates of protection against smallpox are unknown. A

combination of relevant animal efficacy studies along with thorough comparative immunogenicity studies between traditional and new-generation smallpox vaccines will be necessary for vaccine licensure. In the present study, a variety of immune responses elicited by MVA and the licensed smallpox vaccine Dryvax in a murine model were compared, with a focus on mimicking conditions and strategies likely to be employed in human vaccine trials. Immunization of mice with MVA, using several relevant vaccination routes including needle-free delivery, elicited humoral and cellular immune responses qualitatively similar to those elicited by vaccination with Dryvax. Similar levels of vaccinia-specific IgG and neutralizing antibody were elicited by Dryvax and MVA when higher doses (approximately 1 log) of MVA were used for immunization. Antibody levels peaked at about 6 weeks post-immunization and remained stable for at least 15 weeks. A booster immunization of either MVA or Dryvax following an initial priming immunization with MVA resulted in an enhanced IgG titer and neutralizing antibody response. In addition, both Dryvax and various MVA vaccination protocols elicited antibody responses to the extracellular enveloped form of the virus and afforded protection against a lethal intranasal challenge with vaccinia virus WR.

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Keywords

Modified vaccinia virus Ankara; Dryvax; Vaccine immunogenicity; Smallpox vaccination

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