

Review

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Recombinant poxviruses as mucosal vaccine vectors

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The majority of infections initiate their departure from a mucosal surface, such as Human immunodeficiency virus (HIV), a sexually transmitted virus. Therefore, the induction of mucosal immunity is a high priority in the development of vaccines against mucosal pathogens. The selection of an appropriate antigen delivery system is necessary to induce an efficient mucosal immune response. Poxvirus vectors have been the most intensively studied live recombinant vector, and numerous studies have demonstrated their ability to induce mucosal immune responses against foreign expressed antigens. Previous studies have demonstrated that recombinants based on the attenuated modified vaccinia virus Ankara (MVA) vector were effective in inducing protective responses against different respiratory viruses, such as influenza and respiratory syncytial virus, following immunization via mucosal routes. Recent studies performed in the murine and macaque models have shown that recombinant MVA (rMVA) does not only stimulate HIV-specific immunity in the genital and rectal tracts following mucosal delivery, but can also control simian/human immunodeficiency viraemia and disease progression. In addition, a prime-boost vaccination approach against tuberculosis emphasized the importance of the intranasal rMVA antigen delivery to induce protective immunity against *Mycobacterium tuberculosis*. The aim of this review is to summarize the studies employing recombinant poxviruses, specifically rMVA as a mucosal delivery vector. The results demonstrate that rMVAs can activate specific immune responses at mucosal surfaces, and encourage further studies to characterize and improve the MVA mucosal immunogenicity of poxvirus vectors.

Introduction

The majority of human pathogens initiate their infectious process through a mucosal barrier, such as Human immunodeficiency virus (HIV), a sexually transmitted virus. Moreover, the impact of HIV infection on mucosal tissues is emphasized by the rapid and marked depletion of CD4⁺ T cells that reside in the gastrointestinal tract and other mucosal tissues, including the lung and vagina (Brenchley *et al.*, 2004; Mehansru *et al.*, 2004). The mucosal route acquires numerous other viral and bacterial infections with significant epidemiological impact. Examples include other sexually transmitted infections caused by *Chlamydia*, *Neisseria gonorrhoeae* and herpes simplex virus (HSV), gastrointestinal tract infections caused by *Helicobacter pylori*, *Vibrio cholerae*, enterotoxigenic *Escherichia coli*, *Shigella* spp., rotaviruses and caliciviruses, and respiratory infections caused by *Mycoplasma pneumoniae*, influenza virus and respiratory syncytial virus (RSV) (Eriksson &

Holmgren, 2002). These pathogens represent a challenge for the induction of mucosal immunity in the development of effective vaccine strategies. Of major importance is the choice of an effective antigen delivery system capable of inducing a significant immune response at a mucosal site. In this review, we discuss the basis in the development of mucosal vaccines, specifically the use of recombinant modified virus Ankara (rMVA) and other attenuated poxvirus vectors. Emphasis is given to current strategies, in particular, (i) prime-boost approaches that may be used in the future, (ii) manipulation of the virus vector, and (iii) the use of mucosal adjuvants.

Key issues in the development of mucosal vaccines

Mucosal surfaces represent a critical component of the mammalian immunological repertoire. Mucosal-associated lymphoid tissue (MALT) is a highly specialized and compartmentalized system composed of organized and dispersed lymphoid tissues, which has been well defined in the gastrointestinal, respiratory and nasal tracts, with the inductive sites of aggregated lymphoid tissues (such as

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