

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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Recombinant Poxviruses Matthew M. Binns, Geoffrey L. Smith, 1992-05-27 *Recombinant Poxviruses* provides a comprehensive examination of poxviruses with an emphasis on the potential of these viruses as new vaccines. The book considers a wide range of issues involved in producing new genetically engineered live vaccines such as efficacy, safety, stability, cost, host range, immune response, immunization route, use of multivalent vaccines, and need for revaccination. The opening chapter describes the origin of vaccinia virus, its use to eradicate smallpox, and the pathogenesis of poxvirus infections. Subsequent chapters examine the molecular biology of poxviruses, methods of constructing vaccinia virus recombinants, and applications, the use and immune responses induced by poxvirus recombinants as live vaccines, and the important issues of the safety and immunogenicity of vaccinia virus. The book's final two chapters report the progress that has been made developing avipoxviruses and parapoxviruses as candidate recombinant vaccines. *Recombinant Poxviruses* will be a welcome addition to the bookshelves of virologists, microbiologists, infectious disease specialists, and veterinarians.

Vaccinia Virus and Poxvirology Stuart N. Isaacs, 2008-02-03 *The Right Book at the Right Time*. The poxviruses comprise a family of complex DNA viruses that replicate in the cytoplasm of vertebrate or invertebrate cells. Of the eight recognized genera of vertebrate poxviruses, those belonging to the orthopoxvirus genus have been most intensively studied. This group includes variola virus, the agent of smallpox, as well as cowpox virus and vaccinia virus. Jenner's original smallpox vaccine, described in 1798, consisted of live cowpox virus, but vaccinia virus later replaced it. There has been speculation as to the origin of vaccinia virus; the most likely idea is that it is a separate species, possibly originally isolated from a horse and is now extinct or rare in nature. Recent genome sequencing studies confirm the distinctness of variola virus, cowpox virus, and vaccinia virus, and also their very close genetic relationship, which accounts for the cross-protection of smallpox vaccines. The novelty of the smallpox vaccine can be readily appreciated by the time it took about 80 years before the next live vaccine

against rabies was developed and another 50 years for the yellow fever vaccine Moreover the eradication of smallpox in 1977 stands as a unique medical achievement Because of its historical role sma pox vaccination contributed greatly to present concepts of infectious disease immunity and pathogenesis Less well known however are the many other firsts for vaccinia virus Recombinant Raccoon Poxvirus-vectored Feline Vaccines Christopher Kulova Ngichabe,1992 *Recombinant DNA and Biological Warfare* Benoît Dubuis,1994 **Recombinant Vectors in Vaccine Development** Fred Brown,1994 This volume explores the use of recombinant vectors in the development of new vaccines to benefit both human and animal health Emphasis is placed on bacterial and viral vectors and their applications *Enhancing the Safety and Efficacy of Recombinant Vaccinia Virus Vaccines* Fatema Hafizullah Aziz,2001 *Immune Responses to Recombinant Vaccinia Viruses Lacking an Immune-modulating Gene* Paulo Henrique Verardi,1997 *Chemical Abstracts* ,2002 **Microbe Hunters, Then and Now** Hilary Koprowski,Michael B. A. Oldstone,1996 Built upon the foundation of Paul de Kruif s Microbe Hunters written in 1926 but differing in that the conquest unfolds through essays by today s scientists this book not only relates the history but also conveys the excitement felt by the individual researchers themselves These dramatic stories describing major accomplishments and future challenges in medical science serve as a beacon to guide new recruits into the battle for control of microbial diseases and provide personal models for graduate and postdoctoral students currently in biomedical research There are some fine ingredients here and it is good to have them together in a single volume embracing past achievements and current and emerging problems in the control of infectious diseases Especially enjoyed Thomas Weller s account complete with pages of laboratory notebook of his isolation of the agent s of varicella and zoster Bernard Dixon British Medical Journal The authors all distinguished and well known scientists recognize the difficult challenges that lie ahead but in general hold an optimistic view of the outcome of future research Microbe Hunters then and now is both interesting and enjoyable to read a timely sequel to de Kruif s original book and a solid historical document written by the microbe hunters themselves Abner L Notkins Nature Medicine To order call 800 500 8205 or write MEDI ED Press 5 White Place Bloomington IL 61701 Encyclopedia of Virology Brian W. J. Mahy,M. H. V. Van Regenmortel,2008 Covers biological molecular and medical topics concerning viruses in animals plants bacteria and insects this new ed has been extensively revised and updated to reflect the 50 % increase in identified and accepted viruses since 2000 Includes information on avian flu SARS and West Nile and the ability of some viruses to be used as agents of bioterrorism The Evolutionary Biology of Viruses Stephen S. Morse,1994 **Advances in Animal Virology** Dr. Shahid Jameel,Luis P. Villarreal,2000 This volume collects papers presented at the second ICGEB UCI Virology Symposium held in New Delhi in November 1998 Papers include Cellular Pathways of Infection for Moloney Murine Leukaemia Virus and Regulation of HIV 2 Transcription by Pets Binding Factors **Proceedings of the National Academy of Sciences of the United States of America** National Academy of Sciences (U.S.),2004 *Biological and Toxin Weapons Today* Erhard Geissler,1986 As genetic engineering and other

biotechnologies have developed so has the potential for biological and toxin warfare In this book experts from both East and West discuss the development of these powerful agents of mass destruction as well as the creation of vaccines against them Paying particular attention to the provisions of the 1975 Biological Weapons Convention this study concludes with policy recommendations designed to strengthen the treaty and prevent the future military use of bioscience discoveries **RNA GENETICS DIR VIRUS REPLIC** John J. Holland, Paul Ahlquist, 1988-05-31 **AIDS Research and Human Retroviruses**, 1996 **The Onderstepoort Journal of Veterinary Research**, 1994 *Developments in Biological Standardization*, 1974 Consists of proceedings of symposia organized by the International Association of Biological Standardization

Vaccines, Vaccination, and the Immune Response G. L. Ada, Alistair J. Ramsay, 1997 This volume reviews current work on new vaccines and defines the key immunological principles that govern vaccine development The opening section describes current vaccines and those in late stage clinical trials surveys national and international immunization programmes and highlights future needs and opportunities in vaccine development A major portion of the text examines the innate and adaptive immune systems the roles of different immune responses in combatting infection the mechanisms by which infectious agents invade or subvert immune responses and the most effective ways of enhancing or selectively inducing different immune responses The authors also discuss vaccine design including peptide based vaccines rDNA technology genetic DNA preparations and methods for producing vaccine preparations in plants The final section explores the prospects of immunotherapy for tumours autoimmune diseases and fertility control

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