Transgenic And Chimeric Viral Delivery Systems

Published date: Feb. 1, 2012

Technology description

The development of eukaryotic viral vectors has generally focused on delivery of one or more heterologous genes to target cells, particularly for gene therapy. Such development has primarily involved vector systems utilizing retrovirus, adenovirus, herpes virus, vaccinia virus, and adeno-associated virus particles. However, each of these viral vector systems has presented one or more of several obstacles including low viral titers, induced host immune responses, inefficient transduction, and transient expression of the desired heterologous gene. This invention addresses the need for improved eukaryotic viral vectors for diagnostic applications and for delivering heterologous genes to cells in vitro, ex vivo, and in vivo. The present invention provides a system for the production of viral vectors (secondary viruses) whose genome is encoded within another virus with a different life cycle and biologic characteristics (primary virus). For example, chimeric primary viruses with high transduction efficiencies (adenoviruses) can be used to direct the production of secondary viruses (retroviruses) in a wide range of producer cell types. Thus single (or panels of) secondary viral vectors containing identical secondary vector genomes can easily and rapidly be produced in retroviral vector packaging cells containing different envelope targeting components with the additional advantage that there will be little chance for vector rearrangement or recombination. Secondary viruses also can be readily produced in cells obtained from the eventual gene therapy target species so that enveloped viruses will contain membrane constituents from the same, rather than a xenogeneic species, lessening the chance for neutralizing immune responses to the vectors. Similarly, serum complement-mediated lysis of retroviral vectors may be eliminated by the ability to easily use vector producer cells from the same species as the species to be treated by gene therapy. Such secondary viruses may comprise an expression cassette constituting a nucleic acid encoding a heterologous protein and/or an antisense nuclei acid. Hence, this invention overcomes obstacles occurring with the in vitro, ex vivo, and in vivo use of common viral vector systems. In addition, these chimeric primary viruses can be used to rescue unknown viral genomes from host cells for use in the development of diagnostic tests or in the development of novel viral vector systems.

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