[0004] The discovery of the role of DCs as specialized antigen-presenting cells (APCs) has fueled attempts at DC-based immunization/vaccination that involve loading DCs with specific antigens (Banchereau, J. & Palucka, A.K. 2005. *Nat. Rev. Immunol.* 5:296-306; Figdor, C.G. et al. 2004. *Nat. Med.* 10:475-480, each of which is incorporated herein by reference in its entirety). However, all of these attempts involve ex vivo loading of DCs with specific antigens. Ex vivo generated DCs are then administered to the patient. Ex vivo generation of DCs for each patient is extremely labor intensive process.

[0005] By contrast, the present invention is directed *inter alia* to targeting, antigen loading and activation of DCs in vivo, which results in vivo treatment of diseases by generating a beneficial immune response in the patient. The invention thus fulfills a longstanding need for effective and efficient regimes for immunization/vaccination.

SUMMARY OF THE INVENTION

[0005a] In one aspect, there is provided an in vitro method of delivering a lentiviral vector encoding an antigen to a dendritic cell expressing DC-SIGN (Dendritic Cell Specific ICAM-3 (Intracellular Adhesion Molecules 3)-Grabbing Nonintegrin), the method comprising:

transducing the dendritic cell with a recombinant virus, wherein the recombinant virus comprises said lentiviral vector,
wherein the recombinant virus comprises an alphavirus glycoprotein that targets said cell expressing DC-SIGN,
wherein said glycoprotein is an alphavirus E2 glycoprotein mutated at a heparan sulfate binding site to decrease or eliminate its binding to heparan sulfate.

[0005b] In one aspect, there is provided a recombinant virus as defined herein, or a pharmaceutical composition comprising said recombinant virus.

[0005c] In one aspect, there is provided a recombinant virus comprising a lentiviral vector encoding an antigen and an alphavirus glycoprotein that targets cells expressing DC-SIGN wherein said glycoprotein is an alphavirus E2 glycoprotein mutated at a heparan sulfate binding site to decrease or eliminate its binding to heparan sulfate, for use in stimulating an immune response to said antigen in a mammal.

[0005d] In one aspect, there is provided a dendritic cell transduced with a recombinant virus, wherein the recombinant virus is as defined herein.

[0006] In one aspect of the invention methods of delivering a polynucleotide to a dendritic cell expressing DC-SIGN are provided. In some embodiments the methods comprise transducing the dendritic cell with a recombinant virus, wherein the recombinant virus comprises the polynucleotide to be delivered and a targeting molecule that binds DC-SIGN. In some embodiments the targeting molecule is specific for DC-SIGN.

[0007] In some embodiments of the invention, the recombinant virus comprises sequences from a lentivirus genome, such as an HIV genome.

[0008] In other embodiments the recombinant virus comprises sequences from a gammaretrovirus genome, such as sequences from a Mouse Stem Cell Virus (MSCV) genome or a Murine Leukemia Virus (MLV) genome.

[0009] In some embodiments of the invention, the methods utilize a targeting molecule comprising a viral glycoprotein derived from at least one virus selected from the group of: Sindbis virus, influenza virus, Lassa fever virus, tick-borne encephalitis virus, Dengue virus, Hepatitis B virus, Rabies virus, Semliki Forest virus, Ross River virus, Aura virus, Borna disease virus, Hantaan virus, and SARS-CoV virus. In more particular embodiments, the targeting molecule comprises a modified viral glycoprotein derived from Sindbis virus (SIN or SVG). In certain embodiments, the targeting molecule is SINmu also known as SVGmu (SEQ ID NO: 11).