[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).

WHAT IS CLAIMED IS:

1. Use of a replication deficient lentivirus pseudotyped with a virus envelope comprising a modified E2 alphavirus glycoprotein comprising a modification that reduces binding of said E2 to heparan sulfate, wherein the lentivirus comprises a polynucleotide encoding an antigen wherein said polynucleotide is exogenous to the lentivirus genome, and wherein the lentivirus comprising the modified E2 alphavirus glycoprotein more efficiently transduces dendritic cells expressing DC-SIGN relative to cell types not expressing DC-SIGN, in an amount sufficient to elicit an antibody response or antigen-specific T-cell response to the antigen, in the manufacture of a medicament for eliciting an antibody response or antigen-specific T-cell response in a mammal.

2. The use of claim 1 wherein the medicament elicits an antigen-specific T-cell response.

3. The use of claim 2 wherein the medicament elicits an antibody response.

4. The use of claim 2 wherein the replication deficient lentivirus is to be administered subcutaneously.

5. The use of claim 1 wherein the E2 alphavirus glycoprotein is a Sindbis virus glycoprotein.

6. The use of claim 5 wherein the medicament elicits an antigen-specific T-cell response.

7. The use of claim 5 wherein the medicament elicits an antibody response.

8. The use of claim 1 wherein the replication deficient lentivirus is to be administered subcutaneously.

9. The use of claim 5 wherein the replication deficient lentivirus is to be administered subcutaneously.

10. The use of claim 5 wherein the virus envelope further comprises an E1 alphavirus glycoprotein.

11. The use of claim 1 wherein the E2 glycoprotein is produced from the nucleic acid sequence of SEQ ID NO: 3 or comprises the amino acid sequence of SEQ ID NO: 11.

12. The use of claim 5 wherein the lentivirus comprises an HIV sector, a MSCV vector or an MLV vector.

13. The use of claim 1 wherein the replication deficient lentivirus further comprises a polynucleotide encoding a second antigen.

14. The use of claim 5 wherein the replication deficient lentivirus further comprises a polynucleotide encoding a second antigen.

15. The use of claim 5 wherein the mammal is a human.

16. The use of claim 1 wherein the antigen is a tumor associated antigen, viral antigen, bacterial antigen, fungal antigen, protozoan parasite antigen, helminth parasite antigen, or ectoparasite antigen.

17. The use of claim 2 wherein the antigen-specific T-cell response is a $CD8^+$ T-cell response.

18. A recombinant replication deficient lentivirus pseudotyped with a modified E2 alphavirus glycoprotein comprising a modification that reduces binding of said E2 to heparan sulfate, wherein the lentivirus more efficiently transduces dendritic cells expressing DC-SIGN relative to cell types not expressing DC-SIGN; wherein the lentivirus comprises a polynucleotide encoding an antigen wherein said polynucleotide is exogenous to the lentivirus genome, and wherein said lentivirus is capable of eliciting an antibody response or antigen-specific T-cell response to the antigen.

19. The recombinant lentivirus of claim 18, wherein the recombinant lentivirus comprises a sequence from an HIV genome.

20. The recombinant lentivirus of claim 18, wherein the recombinant lentivirus comprises an inactivated or self-inactivating 3' LTR.

21. The recombinant lentivirus of claim 18, wherein the E2 alphavirus glycoprotein comprises the sequence defined by SEQ ID NO: 11.

22. The recombinant lentivirus of claim 18, wherein the antigen is a tumor antigen.

23. The recombinant lentivirus of claim 18, further comprising an E1 alphavirus glycoprotein.

24. The recombinant lentivirus of claim 18, wherein the E2 alphavirus glycoprotein is a Sindbis virus E2 glycoprotein.

25. Use of a replication deficient lentivirus that (a) comprises an exogenous polynucleotide encoding an antigen associated with a disease, and (b) is pseudotyped with a virus envelope comprising modified E2 alphavirus glycoprotein that transduces dendritic cells more efficiently than other cell types, in an amount sufficient to stimulate an immune response to said antigen, in the manufacture of a medicament for stimulating an antigen-specific immune response in a mammal.

26. The use of claim 25 wherein the immune response is an antibody response or antigen-specific T-cell response or both.

27. The use of claim 26 wherein the immune response is an antigen-specific T-cell response.

28. The use of claim 27 wherein the antigen-specific T-cell response is a $CD8^+$ T-cell response.

29. The use of claim 25 wherein the virus envelope further comprises an E1 alphavirus glycoprotein.

30. The use of claim 25 wherein the E2 glycoprotein is produced from the nucleic acid sequence of SEQ ID NO: 3 or comprises the amino acid sequence of SEQ ID NO: 11.

31. The use of claim 25 wherein the lentivirus comprises an HIV vector, a MSCV vector or an MLV vector.

32. The use of claim 25 wherein the replication deficient lentivirus further comprises a polynucleotide encoding a second antigen associated with a disease.

33. The use of claim 25 wherein the mammal is a human.

34. The use of claim 25 wherein the antigen is a tumor associated antigen, viral antigen, bacterial antigen, fungal antigen, protozoan parasite antigen, helminth parasite antigen, or ectoparasite antigen.

35. The use according to claim 34 wherein the antigen is Her-2 receptor, MAGE, BAGE, RAGE, NY-ESO, MART-1/Melan-A, gp100, gp75, mda-7, tyrosinase, tyrosinase-related protein, prostate specific membrane antigen (PSMA), prostate-specific antigen (PSA), ras, bcr/ab1, Her2/neu, p53, cytochrome P450 1B1, N-acetylglucosaminyltransferase-V, human papilloma virus protein E6, human papilloma virus protein E7, carcinoembryonic antigen and alpha-fetoprotein, gp120, an adenovirus polypeptide, an alphavirus polypeptide, a calicivirus polypeptide, calicivirus capsid antigen, a coronavirus polypeptide, s distemper virus polypeptide, an Ebola virus polypeptide, an enterovirus polypeptide, a flavivirus polypeptides, a hepatitis virus (AE) polypeptide, a hepatitis B core antigen, a hepatitis or surface antigen, a herpesvirus polypeptide, a herpes simplex virus glycoptrotein, a varicella zoster virus glycoprotein, an immunodeficiency virus polypeptide, a human immunodeficiency virus envelope protein, a human immunodeficiency virus protease, an infectious peritonitis virus polypeptide, an influenza virus polypeptide, an influenza A hemagglutinin, an influenza A neuraminidase, an influenza A

nucleoprotein, a leukemia virus polypeptide, a Marburg virus polypeptide, an orthomyxovirus polypeptide, a papilloma virus polypeptide, a parainfluenza virus polypeptide, a parainfluenza virus hemagglutinin, aparainfluenza virus neuraminidase, a paramyxovirus polypeptide, a parvovirus polypeptide, a pestivirus polypeptide, a picorna virus polypeptidea poliovirus capsid polypeptide, a pox virus polypeptide, a vaccinia virus polypeptide, a rabies virus polypeptide, a rabies virus glycoprotein G, a reovirus polypeptide, a retrovirus polypeptide, a rotavirus polypeptide, an Absidia polypeptide, an Acremonium polypeptide, an Alternaria polypeptide, an Aspergillus polypeptide, a Basidiobolus polypeptide, a Bipolaris polypeptide, a Blastomyces polypeptide, a Candida polypeptide, a Coccidioides polypeptide, a Conidiobolus polypeptide, a Cryptococcus polypeptide, a Curvalaria polypeptide, an Epidermophyton polypeptide, an Exophiala polypeptide, an Geotrichum polypeptide, a Histoplasma polypeptide, a Madurella polypeptide, a Malassezia polypeptide, a Microsporum polypeptide, a Moniliella polypeptide, a Mortierella polypeptide, a Mucor polypeptide, a Paecilomyces polypeptide, a Penicillium polypeptide, a Phialemonium polypeptide, a Phialophora polypeptide, a Prototheca polypeptide, a Pseudallescheria polypeptide, a Pseudomicrodochium polypeptide, a Pythium polypeptide, a Rhinosporidium polypeptide, a Rhizopus polypeptide, a Scolecobasidium polypeptide, a Sporothrix polypeptide, a Stemphylium polypeptide, a Trichophyton polypeptide, a Trichosporon polypeptide, and a Xylohypha polypeptide, a Babesia polypeptide, a Balantidium polypeptide, a Besnoitia polypeptide, a Cryptosporidium polypeptide, an Eimeria polypeptide, an Encephalitozoon polypeptide, an Entamoeba polypeptide, a Giardia polypeptide, a Hammondia polypeptide, a Hepatozoon polypeptide, an Isospora polypeptide, a Leishmania polypeptide, a Microsporidia polypeptide, a Neospora polypeptide, a Nosema polypeptide, a Pentatrichomonas polypeptide, a Plasmodium polypeptide, P. falciparum circumsporozoite (PfCSP), sporozoite surface protein 2 (PfSSP2), carboxyl terminus of liver state antigen 1 (PfLSA1 c-term), exported protein 1 (PfExp-1), a Pneumocystis polypeptide, a Sarcocystis polypeptide, a Schistosoma polypeptide, Ta heileria polypeptide, a Toxoplasma polypeptide, a Trypanosoma polypeptide, an Acanthocheilonema polypeptide, an Aelurostrongylus polypeptide, an Ancylostoma polypeptide, an Angiostrongylus polypeptide, an Ascaris polypeptide, a Brugia polypeptide, a Bunostomum polypeptide, a Capillaria polypeptide, a Chabertia polypeptide, a Cooperia polypeptide, a Crenosoma polypeptide, a Dictyocaulus polypeptide, a Dioctophyme polypeptide, a Dipetalonema polypeptide, a Diphyllobothrium

polypeptide, a Diplydium polypeptide, a Dirofilaria polypeptide, a Dracunculus polypeptide, an Enterobius polypeptide, a Filaroides polypeptide, a Haemonchus polypeptide, a Lagochilascaris polypeptide, a Loa polypeptide, a Mansonella polypeptide, a Muellerius polypeptide, a Nanophyetus polypeptide, a Necator polypeptide, a Nematodirus polypeptide, an Oesophagostomum polypeptide, an Onchocerca polypeptide, an Opisthorchis polypeptide, ab Ostertagia polypeptide, a Parafilaria polypeptide, a Paragonimus polypeptide, a Parascaris polypeptide, a Physaloptera polypeptide, a Protostrongylus polypeptide, a Setaria polypeptide, a Spirocerca polypeptide, a Spirometra polypeptide, a Stephanofilaria polypeptide, a Strongyloides polypeptide, a Strongylus polypeptide, a Thelazia polypeptide, a Toxascaris polypeptide, a Toxocara polypeptide, a Trichinella polypeptide, a Trichostrongylus polypeptide, a Trichuris polypeptide, an Uncinaria polypeptide, a Wuchereria polypeptide, a flea polypeptide, a tick polypeptide, a hard tick polypeptide, a soft tick polypeptide, a fly polypeptide, a midge polypeptide, a mosquito polypeptide, a sand fly polypeptide, a black fly polypeptide, a horse fly polypeptide, a horn fly polypeptide, a deer fly polypeptide, a tsetse fly polypeptide, a stable fly polypeptide, a myiasis-causing fly polypeptide, a biting gnat polypeptide, an ant polypeptide, a spider polypeptide, a lice polypeptide, a mite polypeptide, a true bug polypeptide, a bed bug polypeptide, and a kissing bug polypeptide.

36. The use of claim 25 wherein the lentivirus further comprises a nucleotide sequence encoding a maturation factor.

37. The use of claim 36 wherein the maturation factor is selected from the group consisting of GM-CSF, 1L-2, 1L-4, 1L-6, 1L-7, IL-15, IL-21, IL-23, TNFα, B7.1, B7.2, 4-1BB, CD40 ligand (CD4OL) and drug-inducible CD40 (iCD40).

38. The use of claim 25 wherein the replication deficient lentivirus is administered subcutaneously or intradermally.

39. The use of claim 25 wherein the E2 alphavirus glycoprotein is a Sindbis virus glycoprotein.

40. The use of claim 39 wherein the replication deficient lentivirus is administered subcutaneously or intradermally.

41. The use of claim 39 wherein the lentivirus comprises an HIV vector, a MSCV vector or an MLV vector.

42. The use of claim 39 wherein the replication deficient lentivirus further comprises a polynucleotide encoding a second antigen associated with a disease.

43. The use of claim 39 wherein the mammal is a human.

44. The use of claim 39 wherein the antigen is a tumor associated antigen, viral antigen, bacterial antigen, fungal antigen, protozoan parasite antigen, helminth parasite antigen, or ectoparasite antigen.

45. The use according to claim 44 wherein the antigen is Her-2 receptor, MAGE, BAGE, RAGE, NY-ESO, MART-1/Melan-A, gp100, gp75, mda-7, tyrosinase, tyrosinase-related protein, prostate specific membrane antigen (PSMA), prostate-specific antigen (PSA), ras, bcr/ab1, Her2/neu, p53, cytochrome P450 1B1, N-acetylglucosaminyltransferase-V, human papilloma virus protein E6, human papilloma virus protein E7, carcinoembryonic antigen and alpha-fetoprotein, gp120, an adenovirus polypeptide, an alphavirus polypeptide, a calicivirus polypeptide, calicivirus capsid antigen, a coronavirus polypeptide, s distemper virus polypeptide, an Ebola virus polypeptide, an enterovirus polypeptide, a flavivirus polypeptides, a hepatitis virus (AE) polypeptide, a hepatitis B core antigen, a hepatitis or surface antigen, a herpesvirus polypeptide, a herpes simplex virus glycoptrotein, a varicella zoster virus glycoprotein, an immunodeficiency virus polypeptide, a human immunodeficiency virus envelope protein, a human immunodeficiency virus protease, an infectious peritonitis virus polypeptide, an influenza virus polypeptide, an influenza A hemagglutinin, an influenza A neuraminidase, an influenza A nucleoprotein, a leukemia virus polypeptide, a Marburg virus polypeptide, an orthomyxovirus polypeptide, a papilloma virus polypeptide, a parainfluenza virus polypeptide, a parainfluenza virus hemagglutinin, aparainfluenza virus neuraminidase, a paramyxovirus polypeptide, a parvovirus polypeptide, a pestivirus polypeptide, a picorna virus polypeptidea poliovirus capsid polypeptide, a pox virus polypeptide, a vaccinia virus polypeptide, a rabies virus polypeptide, a rabies virus glycoprotein G, a reovirus polypeptide, a retrovirus polypeptide, a rotavirus polypeptide, an Absidia polypeptide, an Acremonium polypeptide, an Alternaria polypeptide, an Aspergillus polypeptide, a Basidiobolus polypeptide, a Bipolaris polypeptide, a Blastomyces

polypeptide, a Candida polypeptide, a Coccidioides polypeptide, a Conidiobolus polypeptide, a Cryptococcus polypeptide, a Curvalaria polypeptide, an Epidermophyton polypeptide, an Exophiala polypeptide, an Geotrichum polypeptide, a Histoplasma polypeptide, a Madurella polypeptide, a Malassezia polypeptide, a Microsporum polypeptide, a Moniliella polypeptide, a Mortierella polypeptide, a Mucor polypeptide, a Paecilomyces polypeptide, a Penicillium polypeptide, a Phialemonium polypeptide, a Phialophora polypeptide, a Prototheca polypeptide, a Pseudallescheria polypeptide, a Pseudomicrodochium polypeptide, a Pythium polypeptide, a Rhinosporidium polypeptide, a Rhizopus polypeptide, a Scolecobasidium polypeptide, a Sporothrix polypeptide, a Stemphylium polypeptide, a Trichophyton polypeptide, a Trichosporon polypeptide, and a Xylohypha polypeptide, a Babesia polypeptide, a Balantidium polypeptide, a Besnoitia polypeptide, a Cryptosporidium polypeptide, an Eimeria polypeptide, an Encephalitozoon polypeptide, an Entamoeba polypeptide, a Giardia polypeptide, a Hammondia polypeptide, a Hepatozoon polypeptide, an Isospora polypeptide, a Leishmania polypeptide, a Microsporidia polypeptide, a Neospora polypeptide, a Nosema polypeptide, a Pentatrichomonas polypeptide, a Plasmodium polypeptide, P. falciparum circumsporozoite (PfCSP), sporozoite surface protein 2 (PfSSP2), carboxyl terminus of liver state antigen 1 (PfLSA1 c-term), exported protein 1 (PfExp-1), a Pneumocystis polypeptide, a Sarcocystis polypeptide, a Schistosoma polypeptide, Ta heileria polypeptide, a Toxoplasma polypeptide, a Trypanosoma polypeptide, an Acanthocheilonema polypeptide, an Aelurostrongylus polypeptide, an Ancylostoma polypeptide, an Angiostrongylus polypeptide, an Ascaris polypeptide, a Brugia polypeptide, a Bunostomum polypeptide, a Capillaria polypeptide, a Chabertia polypeptide, a Cooperia polypeptide, a Crenosoma polypeptide, a Dictyocaulus polypeptide, a Dioctophyme polypeptide, a Dipetalonema polypeptide, a Diphyllobothrium polypeptide, a Diplydium polypeptide, a Dirofilaria polypeptide, a Dracunculus polypeptide, an Enterobius polypeptide, a Filaroides polypeptide, a Haemonchus polypeptide, a Lagochilascaris polypeptide, a Loa polypeptide, a Mansonella polypeptide, a Muellerius polypeptide, a Nanophyetus polypeptide, a Necator polypeptide, a Nematodirus polypeptide, an Oesophagostomum polypeptide, an Onchocerca polypeptide, an Opisthorchis polypeptide, ab Ostertagia polypeptide, a Parafilaria polypeptide, a Paragonimus polypeptide, a Parascaris polypeptide, a Physaloptera polypeptide, a Protostrongylus polypeptide, a Setaria polypeptide, a Spirocerca polypeptide, a Spirometra polypeptide, a Stephanofilaria polypeptide, a Strongyloides

polypeptide, a Strongylus polypeptide, a Thelazia polypeptide, a Toxascaris polypeptide, a Toxocara polypeptide, a Trichinella polypeptide, a Trichostrongylus polypeptide, a Trichuris polypeptide, an Uncinaria polypeptide, a Wuchereria polypeptide, a flea polypeptide, a tick polypeptide, a hard tick polypeptide, a soft tick polypeptide, a fly polypeptide, a midge polypeptide, a mosquito polypeptide, a sand fly polypeptide, a black fly polypeptide, a horse fly polypeptide, a horn fly polypeptide, a deer fly polypeptide, a tsetse fly polypeptide, a stable fly polypeptide, a myiasis-causing fly polypeptide, a biting gnat polypeptide, an ant polypeptide, a spider polypeptide, a lice polypeptide, a mite polypeptide, a true bug polypeptide, a bed bug polypeptide, and a kissing bug polypeptide.

46. The use of claim 39 wherein the lentivirus further comprises a nucleotide sequence encoding a maturation factor.

47. A recombinant replication deficient lentivirus pseudotyped with a modified E2 alphavirus glycoprotein that more efficiently transduces dendritic cells compared to other cell types; wherein the lentivirus comprises an exogenous polynucleotide encoding an antigen associated with a disease, and wherein said lentivirus is capable of stimulating an immune response to said antigen.

48. The recombinant lentivirus of claim 47, wherein the recombinant lentivirus comprises an inactivated or self-inactivating 3' LTR.

49. The recombinant lentivirus of claim 47 wherein the immune response is an antibody response or antigen-specific T-cell response or both.

50. The recombinant lentivirus of claim 49 wherein the immune response is an antigen-specific T-cell response.

51. The recombinant lentivirus of claim 50 wherein the antigen-specific T-cell response is a $CD8^+$ T-cell response.

52. The recombinant lentivirus of claim 47 wherein the virus envelope further comprises an E1 alphavirus glycoprotein.

53. The recombinant lentivirus of claim 47 wherein the E2 glycoprotein is produced from the nucleic acid sequence of SEQ ID NO: 3 or comprises the amino acid sequence of SEQ ID NO: 11.

54. The recombinant lentivirus of claim 47 wherein the lentivirus comprises an HIV vector, a MSCV vector or an MLV vector.

55. The recombinant lentivirus of claim 47 wherein the replication deficient lentivirus further comprises a polynucleotide encoding a second antigen associated with a disease.

56. The recombinant lentivirus of claim 47 wherein the antigen is a tumor associated antigen, viral antigen, bacterial antigen, fungal antigen, protozoan parasite antigen, helminth parasite antigen, or ectoparasite antigen.

57. The recombinant lentivirus of claim 56 wherein the antigen is Her-2 receptor, MAGE, BAGE, RAGE, NY-ESO, MART-1/Melan-A, gp100, gp75, mda-7, tyrosinase, tyrosinase-related protein, prostate specific membrane antigen (PSMA), prostate-specific antigen (PSA), ras, bcr/abl, Her2/neu, p53, cytochrome P450 1B1, N-acetylglucosaminyltransferase-V, human papilloma virus protein E6, human papilloma virus protein E7, carcinoembryonic antigen and alpha-fetoprotein, gp120, an adenovirus polypeptide, an alphavirus polypeptide, a calicivirus polypeptide, calicivirus capsid antigen, a coronavirus polypeptide, s distemper virus polypeptide, an Ebola virus polypeptide, an enterovirus polypeptide, a flavivirus polypeptides, a hepatitis virus (AE) polypeptide, a hepatitis B core antigen, a hepatitis or surface antigen, a herpesvirus polypeptide, a herpes simplex virus glycoptrotein, a varicella zoster virus glycoprotein, an immunodeficiency virus polypeptide, a human immunodeficiency virus envelope protein, a human immunodeficiency virus protease, an infectious peritonitis virus polypeptide, an influenza virus polypeptide, an influenza A hemagglutinin, an influenza A neuraminidase, an influenza A nucleoprotein, a leukemia virus polypeptide, a Marburg virus polypeptide, an orthomyxovirus polypeptide, a papilloma virus polypeptide, a parainfluenza virus polypeptide, a parainfluenza virus hemagglutinin, aparainfluenza virus neuraminidase, a paramyxovirus polypeptide, a parvovirus polypeptide, a pestivirus polypeptide, a picorna virus polypeptidea poliovirus capsid polypeptide, a pox virus polypeptide, a vaccinia virus polypeptide, a rabies virus polypeptide, a rabies virus glycoprotein G, a reovirus polypeptide, a retrovirus polypeptide, a rotavirus polypeptide, an Absidia polypeptide, an Acremonium polypeptide, an Alternaria polypeptide, an Aspergillus polypeptide, a Basidiobolus polypeptide, a Bipolaris polypeptide, a Blastomyces polypeptide, a Candida polypeptide, a Coccidioides polypeptide, a Conidiobolus polypeptide, a Cryptococcus polypeptide, a Curvalaria polypeptide, an Epidermophyton polypeptide, an

Exophiala polypeptide, an Geotrichum polypeptide, a Histoplasma polypeptide, a Madurella polypeptide, a Malassezia polypeptide, a Microsporum polypeptide, a Moniliella polypeptide, a Mortierella polypeptide, a Mucor polypeptide, a Paecilomyces polypeptide, a Penicillium polypeptide, a Phialemonium polypeptide, a Phialophora polypeptide, a Prototheca polypeptide, a Pseudallescheria polypeptide, a Pseudomicrodochium polypeptide, a Pythium polypeptide, a Rhinosporidium polypeptide, a Rhizopus polypeptide, a Scolecobasidium polypeptide, a Sporothrix polypeptide, a Stemphylium polypeptide, a Trichophyton polypeptide, a Trichosporon polypeptide, and a Xylohypha polypeptide, a Babesia polypeptide, a Balantidium polypeptide, a Besnoitia polypeptide, a Cryptosporidium polypeptide, an Eimeria polypeptide, an Encephalitozoon polypeptide, an Entamoeba polypeptide, a Giardia polypeptide, a Hammondia polypeptide, a Hepatozoon polypeptide, an Isospora polypeptide, a Leishmania polypeptide, a Microsporidia polypeptide, a Neospora polypeptide, a Nosema polypeptide, a Pentatrichomonas polypeptide, a Plasmodium polypeptide, P. falciparum circumsporozoite (PfCSP), sporozoite surface protein 2 (PfSSP2), carboxyl terminus of liver state antigen 1 (PfLSA1 c-term), exported protein 1 (PfExp-1), a Pneumocystis polypeptide, a Sarcocystis polypeptide, a Schistosoma polypeptide, Ta heileria polypeptide, a Toxoplasma polypeptide, a Trypanosoma polypeptide, an Acanthocheilonema polypeptide, an Aelurostrongylus polypeptide, an Ancylostoma polypeptide, an Angiostrongylus polypeptide, an Ascaris polypeptide, a Brugia polypeptide, a Bunostomum polypeptide, a Capillaria polypeptide, a Chabertia polypeptide, a Cooperia polypeptide, a Crenosoma polypeptide, a Dictyocaulus polypeptide, a Dioctophyme polypeptide, a Dipetalonema polypeptide, a Diphyllobothrium polypeptide, a Diplydium polypeptide, a Dirofilaria polypeptide, a Dracunculus polypeptide, an Enterobius polypeptide, a Filaroides polypeptide, a Haemonchus polypeptide, a Lagochilascaris polypeptide, a Loa polypeptide, a Mansonella polypeptide, a Muellerius polypeptide, a Nanophyetus polypeptide, a Necator polypeptide, a Nematodirus polypeptide, an Oesophagostomum polypeptide, an Onchocerca polypeptide, an Opisthorchis polypeptide, ab Ostertagia polypeptide, a Parafilaria polypeptide, a Paragonimus polypeptide, a Parascaris polypeptide, a Physaloptera polypeptide, a Protostrongylus polypeptide, a Setaria polypeptide, a Spirocerca polypeptide, a Spirometra polypeptide, a Stephanofilaria polypeptide, a Strongyloides polypeptide, a Strongylus polypeptide, a Thelazia polypeptide, a Toxascaris polypeptide, a Toxocara polypeptide, a Trichinella polypeptide, a Trichostrongylus polypeptide, a Trichuris polypeptide, an Uncinaria

polypeptide, a Wuchereria polypeptide, a flea polypeptide, a tick polypeptide, a hard tick polypeptide, a soft tick polypeptide, a fly polypeptide, a midge polypeptide, a mosquito polypeptide, a sand fly polypeptide, a black fly polypeptide, a horse fly polypeptide, a horn fly polypeptide, a deer fly polypeptide, a tsetse fly polypeptide, a stable fly polypeptide, a myiasis-causing fly polypeptide, a biting gnat polypeptide, an ant polypeptide, a spider polypeptide, a lice polypeptide, a mite polypeptide, a true bug polypeptide, a bed bug polypeptide, and a kissing bug polypeptide.

58. The recombinant lentivirus of claim 47 wherein the lentivirus further comprises a nucleotide sequence encoding a maturation factor.

59. The recombinant lentivirus of claim 58 wherein the maturation factor is selected from the group consisting of GM-CSF, 1L-2, 1L-4, 1L-6, 1L-7, IL-15, IL-21, IL-23, TNFα, B7.1, B7.2, 4-1BB, CD40 ligand (CD4OL) and drug-inducible CD40 (iCD40).

60. The recombinant lentivirus of claim 47 wherein the E2 alphavirus glycoprotein is a Sindbis virus glycoprotein.

61. The recombinant lentivirus of claim 60 wherein the lentivirus comprises an HIV vector, a MSCV vector or an MLV vector.

62. The recombinant lentivirus of claim 60 wherein the replication deficient lentivirus further comprises a polynucleotide encoding a second antigen associated with a disease.

63. The recombinant lentivirus of claim 60 wherein the antigen is a tumor associated antigen, viral antigen, bacterial antigen, fungal antigen, protozoan parasite antigen, helminth parasite antigen, or ectoparasite antigen.

64. The recombinant lentivirus of claim 63 wherein the antigen is Her-2 receptor, MAGE, BAGE, RAGE, NY-ESO, MART-1/Melan-A, gp100, gp75, mda-7, tyrosinase, tyrosinase-related protein, prostate specific membrane antigen (PSMA), prostate-specific antigen (PSA), ras, bcr/ab1, Her2/neu, p53, cytochrome P450 1B1, N-acetylglucosaminyltransferase-V, human papilloma virus protein E6, human papilloma virus protein E7, carcinoembryonic antigen and alpha-fetoprotein, gp120, an adenovirus polypeptide, an alphavirus polypeptide, a calicivirus polypeptide, calicivirus capsid antigen, a coronavirus polypeptide, s distemper virus polypeptide, an Ebola virus polypeptide, an enterovirus polypeptide, a flavivirus polypeptides, a hepatitis

virus (AE) polypeptide, a hepatitis B core antigen, a hepatitis or surface antigen, a herpesvirus polypeptide, a herpes simplex virus glycoptrotein, a varicella zoster virus glycoprotein, an immunodeficiency virus polypeptide, a human immunodeficiency virus envelope protein, a human immunodeficiency virus protease, an infectious peritonitis virus polypeptide, an influenza virus polypeptide, an influenza A hemagglutinin, an influenza A neuraminidase, an influenza A nucleoprotein, a leukemia virus polypeptide, a Marburg virus polypeptide, an orthomyxovirus polypeptide, a papilloma virus polypeptide, a parainfluenza virus polypeptide, a parainfluenza virus hemagglutinin, aparainfluenza virus neuraminidase, a paramyxovirus polypeptide, a parvovirus polypeptide, a pestivirus polypeptide, a picorna virus polypeptidea poliovirus capsid polypeptide, a pox virus polypeptide, a vaccinia virus polypeptide, a rabies virus polypeptide, a rabies virus glycoprotein G, a reovirus polypeptide, a retrovirus polypeptide, a rotavirus polypeptide, an Absidia polypeptide, an Acremonium polypeptide, an Alternaria polypeptide, an Aspergillus polypeptide, a Basidiobolus polypeptide, a Bipolaris polypeptide, a Blastomyces polypeptide, a Candida polypeptide, a Coccidioides polypeptide, a Conidiobolus polypeptide, a Cryptococcus polypeptide, a Curvalaria polypeptide, an Epidermophyton polypeptide, an Exophiala polypeptide, an Geotrichum polypeptide, a Histoplasma polypeptide, a Madurella polypeptide, a Malassezia polypeptide, a Microsporum polypeptide, a Moniliella polypeptide, a Mortierella polypeptide, a Mucor polypeptide, a Paecilomyces polypeptide, a Penicillium polypeptide, a Phialemonium polypeptide, a Phialophora polypeptide, a Prototheca polypeptide, a Pseudallescheria polypeptide, a Pseudomicrodochium polypeptide, a Pythium polypeptide, a Rhinosporidium polypeptide, a Rhizopus polypeptide, a Scolecobasidium polypeptide, a Sporothrix polypeptide, a Stemphylium polypeptide, a Trichophyton polypeptide, a Trichosporon polypeptide, and a Xylohypha polypeptide, a Babesia polypeptide, a Balantidium polypeptide, a Besnoitia polypeptide, a Cryptosporidium polypeptide, an Eimeria polypeptide, an Encephalitozoon polypeptide, an Entamoeba polypeptide, a Giardia polypeptide, a Hammondia polypeptide, a Hepatozoon polypeptide, an Isospora polypeptide, a Leishmania polypeptide, a Microsporidia polypeptide, a Neospora polypeptide, a Nosema polypeptide, a Pentatrichomonas polypeptide, a Plasmodium polypeptide, P. falciparum circumsporozoite (PfCSP), sporozoite surface protein 2 (PfSSP2), carboxyl terminus of liver state antigen 1 (PfLSA1 c-term), exported protein 1 (PfExp-1), a Pneumocystis polypeptide, a Sarcocystis polypeptide, a Schistosoma polypeptide, Ta heileria polypeptide, a Toxoplasma polypeptide, a Trypanosoma polypeptide, an

Acanthocheilonema polypeptide, an Aelurostrongylus polypeptide, an Ancylostoma polypeptide, an Angiostrongylus polypeptide, an Ascaris polypeptide, a Brugia polypeptide, a Bunostomum polypeptide, a Capillaria polypeptide, a Chabertia polypeptide, a Cooperia polypeptide, a Crenosoma polypeptide, a Dictyocaulus polypeptide, a Dioctophyme polypeptide, a Dipetalonema polypeptide, a Diphyllobothrium polypeptide, a Diplydium polypeptide, a Dirofilaria polypeptide, a Dracunculus polypeptide, an Enterobius polypeptide, a Filaroides polypeptide, a Haemonchus polypeptide, a Lagochilascaris polypeptide, a Loa polypeptide, a Mansonella polypeptide, a Muellerius polypeptide, a Nanophyetus polypeptide, a Necator polypeptide, a Nematodirus polypeptide, an Oesophagostomum polypeptide, an Onchocerca polypeptide, an Opisthorchis polypeptide, ab Ostertagia polypeptide, a Parafilaria polypeptide, a Paragonimus polypeptide, a Parascaris polypeptide, a Physaloptera polypeptide, a Protostrongylus polypeptide, a Setaria polypeptide, a Spirocerca polypeptide, a Spirometra polypeptide, a Stephanofilaria polypeptide, a Strongyloides polypeptide, a Strongylus polypeptide, a Thelazia polypeptide, a Toxascaris polypeptide, a Toxocara polypeptide, a Trichinella polypeptide, a Trichostrongylus polypeptide, a Trichuris polypeptide, an Uncinaria polypeptide, a Wuchereria polypeptide, a flea polypeptide, a tick polypeptide, a hard tick polypeptide, a soft tick polypeptide, a fly polypeptide, a midge polypeptide, a mosquito polypeptide, a sand fly polypeptide, a black fly polypeptide, a horse fly polypeptide, a horn fly polypeptide, a deer fly polypeptide, a tsetse fly polypeptide, a stable fly polypeptide, a myiasis-causing fly polypeptide, a biting gnat polypeptide, an ant polypeptide, a spider polypeptide, a lice polypeptide, a mite polypeptide, a true bug polypeptide, a bed bug polypeptide, and a kissing bug polypeptide.

65. The recombinant lentivirus of claim 60 wherein the lentivirus further comprises a nucleotide sequence encoding a maturation factor.

WHAT IS CLAIMED IS:

1. 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.

2. The method of claim 1, wherein said glycoprotein is a Sindbis E2 glycoprotein mutated at a heparan sulfate binding site.

3. The method of claim 2, wherein the virus comprises a Sindbis E1 protein and said Sindbis E2 protein and optionally (a) comprises sequences from a murine leukemia virus (MLV) genome or from a human immunodeficiency virus (HIV) genome, and/or (b) encodes a tumor antigen or an HIV antigen.

4. A recombinant virus as defined in any one of claims 1 to 3, or a pharmaceutical composition comprising said recombinant virus.

5. 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.

6. The recombinant virus for use according to claim 5 wherein said glycoprotein is a Sindbis E2 glycoprotein mutated at a heparan sulfate binding site.

7. The recombinant virus for use according to claim 5 or 6, wherein the mammal is human.

8. The recombinant virus for use according to claim 5, 6 or 7, wherein the virus comprises a Sindbis E1 protein and said Sindbis E2 protein.

9. The recombinant virus for use according to claim any one of claims 5 to 8, wherein the lentiviral vector comprises sequences from a Murine Leukemia Virus (MLV) genome or from an HIV genome.

10. The recombinant virus for use according to any one of claims 5 to 9, wherein the antigen is a tumour antigen or an HIV antigen.

11. The recombinant virus for use according to any one of claims 5 to 10, wherein the recombinant virus encodes a second gene of interest, such as a maturation factor selected from the group consisting of GM-CSF, IL-2, IL-4, IL-6, IL-7, IL-15, IL-21, IL-23, TNFα, B7.1, B7.2, 4-1 BB, CD40 ligand (CD40L) and drug-inducible CD40 (iCD40).

12. A dendritic cell transduced with a recombinant virus, wherein the recombinant virus is as defined in any one of claims 1 to 3.

13. The recombinant virus for use according to claim 5 wherein the antigen is a tumor associated antigen, viral antigen, bacterial antigen, fungal antigen, protozoan parasite antigen, helminth parasite antigen, or ectoparasite antigen.

14. The recombinant virus for use according to claim 13,

wherein said tumor associated antigen is selected from the group consisting of Her-2 receptor, MAGE, BAGE, RAGE, and NY-ESO, MART-1/Melan-A, gp100, gp75, mda-7, tyrosinase and tyrosinase-related protein, prostate specific membrane antigen (PSMA), prostate-specific antigen (PSA), mutated ras, bcr/abl rearrangement, Her2/neu, mutated or wild-type p53, cytochrome P450 1B1, N-acetylglucosaminyltransferase-V; human papilloma virus proteins E6 and E7; carcinoembryonic antigen and alpha-fetoprotein;
wherein said viral antigen is selected from the group consisting of adenovirus polypeptides, alphavirus polypeptides, calicivirus polypeptides, calicivirus capsid antigen, coronavirus polypeptides, distemper virus polypeptides, Ebola virus polypeptides, enterovirus polypeptides, flavivirus polypeptides, hepatitis virus (AE) polypeptides, hepatitis B core or surface antigen, herpesvirus polypeptides, herpes simplex virus glycoprotein, varicella zoster virus glycoprotein, immunodeficiency virus polypeptides, human immunodeficiency virus envelope or protease, infectious peritonitis virus polypeptides, influenza virus polypeptides, influenza A hemagglutinin, influenza A neuraminidase, influenza A nucleoprotein, leukemia virus polypeptides, Marburg virus polypeptides, orthomyxovirus polypeptides, papilloma virus polypeptides, parainfluenza virus polypeptides, parainfluenza virus hemagglutinin/neuraminidase, paramyxovirus polypeptides, parvovirus polypeptides, pestivirus polypeptides, picorna virus polypeptides, poliovirus capsid polypeptide, pox virus polypeptides, vaccinia virus polypeptide, rabies virus polypeptides, rabies virus glycoprotein G, reovirus polypeptides, retrovirus polypeptides, and rotavirus polypeptides;
wherein said bacterial antigen is selected from the group consisting of Actinomyces polypeptides, Bacillus polypeptides, Bacteroides polypeptides, Bordetella polypeptides, Bartonella polypeptides, Borrelia polypeptides, B. burgdorferi OspA, Brucella polypeptides, Campylobacter polypeptides, Capnocytophaga polypeptides, Chlamydia polypeptides, Clostridium polypeptides, Corynebacterium polypeptides, Coxiella polypeptides, Dermatophilus polypeptides, Enterococcus polypeptides, Ehrlichia polypeptides, Escherichia polypeptides, Francisella polypeptides, Fusobacterium polypeptides, Haemobartonella polypeptides, Haemophilus polypeptides, H. influenzae type b outer membrane protein, Helicobacter polypeptides, Klebsiella polypeptides, L-form bacteria polypeptides, Leptospira polypeptides, Listeria polypeptides, Mycobacteria polypeptides, Mycoplasma polypeptides, Neisseria polypeptides, Neorickettsia polypeptides, Nocardia polypeptides, Pasteurella polypeptides, Peptococcus polypeptides, Peptostreptococcus polypeptides, Pneumococcus polypeptides, Proteus polypeptides, Pseudomonas polypeptides, Rickettsia polypeptides, Rochalimaea polypeptides, Salmonella polypeptides, Shigella polypeptides, Staphylococcus polypeptides, Streptococcus polypeptides, S. pyogenes M proteins, Treponema polypeptides, andYersinia polypeptides, Y. pestis F1 antigen and Y. pestis V antigen;
wherein said fungal antigen is selected from the group consisting of Absidia polypeptides, Acremonium polypeptides, Alternaria polypeptides, Aspergillus polypeptides, Basidiobolus polypeptides, Bipolaris polypeptides, Blastomyces polypeptides, Candida

polypeptides, Coccidioides polypeptides, Conidiobolus polypeptides, Cryptococcus polypeptides, Curvalaria polypeptides, Epidermophyton polypeptides, Exophiala polypeptides, Geotrichum polypeptides, Histoplasma polypeptides, Madurella polypeptides, Malassezia polypeptides, Microsporum polypeptides, Moniliella polypeptides, Mortierella polypeptides, Mucor polypeptides, Paecilomyces polypeptides, Penicillium polypeptides, Phialemonium polypeptides, Phialophora polypeptides, Prototheca polypeptides, Pseudallescheria polypeptides, Pseudomicrodochium polypeptides, Pythium polypeptides, Rhinosporidium polypeptides, Rhizopus polypeptides, Scolecobasidium polypeptides, Sporothrix polypeptides, Stemphylium polypeptides, Trichophyton polypeptides, Trichosporon polypeptides, and Xylohypha polypeptides;

wherein said protozoan antigen is selected from the group consisting of Babesia polypeptides, Balantidium polypeptides, Besnoitia polypeptides, Cryptosporidium polypeptides, Eimeria polypeptides, Encephalitozoon polypeptides, Entamoeba polypeptides, Giardia polypeptides, Hammondia polypeptides, Hepatozoon polypeptides, Isospora polypeptides, Leishmania polypeptides, Microsporidia polypeptides, Neospora polypeptides, Nosema polypeptides, Pentatrichomonas polypeptides, Plasmodium polypeptides, P. falciparum circumsporozoite (PfCSP), sporozoite surface protein 2 (PfSSP2), carboxyl terminus of liver state antigen 1 (PfLSA1 c-term), exported protein 1 (PfExp-1), Pneumocystis polypeptides, Sarcocystis polypeptides, Schistosoma polypeptides, Theileria polypeptides, Toxoplasma polypeptides, and Trypanosoma polypeptides;

wherein said helminth antigen is selected from the group consisting of Acanthocheilonema polypeptides, Aelurostrongylus polypeptides, Ancylostoma polypeptides, Angiostrongylus polypeptides, Ascaris polypeptides, Brugia polypeptides, Bunostomum polypeptides, Capillaria polypeptides, Chabertia polypeptides, Cooperia polypeptides, Crenosoma polypeptides, Dictyocaulus polypeptides, Dioctophyme polypeptides, Dipetalonema polypeptides, Diphyllobothrium polypeptides, Diplydium polypeptides, Dirofilaria polypeptides, Dracunculus polypeptides, Enterobius polypeptides, Filaroides polypeptides, Haemonchus polypeptides, Lagochilascaris polypeptides, Loa polypeptides, Mansonella polypeptides, Muellerius polypeptides, Nanophyetus polypeptides, Necator polypeptides, Nematodirus polypeptides, Oesophagostomum polypeptides, Onchocerca polypeptides, Opisthorchis polypeptides, Ostertagia polypeptides, Parafilaria polypeptides, Paragonimus polypeptides, Parascaris polypeptides, Physaloptera polypeptides, Protostrongylus polypeptides, Setaria polypeptides, Spirocerca polypeptides Spirometra polypeptides, Stephanofilaria polypeptides, Strongyloides polypeptides, Strongylus polypeptides, Thelazia polypeptides, Toxascaris polypeptides, Toxocara polypeptides, Trichinella polypeptides, Trichostrongylus polypeptides, Trichuris polypeptides, Uncinaria polypeptides, and Wuchereria polypeptides; and wherein said ectoparasite antigen is selected from the group consisting of flea polypeptides; tick polypeptides, hard tick polypeptides, soft tick polypeptides; fly polypeptides, midge polypeptides, mosquito polypeptides, sand fly polypeptides, black fly polypeptides, horse fly polypeptides, horn fly polypeptides, deer fly polypeptides, tsetse fly polypeptides, stable fly polypeptides, myiasis-causing fly polypeptides and biting gnat fly polypeptides; ant fly polypeptides; spider fly polypeptides, lice fly polypeptides; mite fly polypeptides; bed bug fly polypeptides and kissing bug fly polypeptides.

15. The recombinant virus for use according to claim 5 wherein the recombinant virus is administered subcutaneously or intradermally.