can be expanded in relation to the therapeutic strategies to deal with.

Summary

In one aspect, there is provided a use of an expression vector comprising a polynucleotide encoding a fusion protein, said fusion protein comprising (i) human HIV-1 Nef protein with mutations 3C, 153L and 177G, fused at its C-terminus to (ii) an immunogenic antigen in the manufacture of a medicament for the prevention and treatment of disease in a patient, wherein such diseases are known to be mediated by CD8+ T cell response, wherein the medicament is to be administered by intramuscular injection into said patient; and optionally further comprises one or more pharmaceutically acceptable excipients and/or adjuvants.

~~In another aspect, there is provided a use of the expression vector as described herein in the manufacture of a medicament for the prevention and treatment of diseases chosen from the group consisting of chronic infective diseases such as HBV, HCV and HIV, tuberculosis and malaria, acute infective diseases such as influenza, West Nile, Crimean-Congo hemorrhagic fever and Ebola diseases, tumors such as breast, pulmonary, prostate or bladder tumor, wherein the medicament is to be administered by intramuscular injection.~~

In another aspect, there is provided a vaccine composition for use as a vaccine for diseases known to be mediated by CD8+ T cell response, comprising ~~or consisting~~ of an expression vector comprising a polynucleotide encoding a fusion protein, said fusion protein comprising ~~or consisting~~ of (i) human HIV-1 Nef protein with mutations 3C, 153L and 177G, fused at its C-terminus to (ii) an immunogenic antigen, wherein the vaccine composition is to be administered by intramuscular injection; and optionally further comprises one or more pharmaceutically acceptable excipients and/or adjuvants.

~~In another aspect, there is provided a vaccine composition as described herein, for use as a vaccine.~~

In another aspect, there is provided an expression vector comprising a polynucleotide encoding a fusion protein, said fusion protein comprising (i) human HIV-1 Nef protein with mutations 3C, 153L and 177G, fused at its C-terminus to (ii) an immunogenic antigen ~~as described herein~~ for use as a vaccine for diseases known to be mediated by CD8+ T cell response, wherein the expression vector is ~~in a form suitable for~~to be administered ~~administration~~ by intramuscular injection.

In another aspect, there is provided a use of the vaccine composition as described herein in the manufacture of a medicament for the prevention and treatment of a disease~~s~~ chosen from the group consisting of chronic infective diseases ~~such as HBV, HCV and HIV, tuberculosis and malaria~~, acute infective diseases ~~such as influenza, West Nile, Crimean-Congo hemorrhagic fever and Ebola diseases~~, and tumors ~~such as breast, pulmonary, prostate or bladder tumor~~, wherein such diseases are known to be mediated by CD8+ T cell response, and wherein the medicament is to be administered by intramuscular injection.

Detailed Description

It is therefore specific object of the present invention a nucleotide sequence expressing a fusion protein, said fusion protein comprising or consisting of the exosome-anchoring protein of sequence SEQ ID NO:1 fused at its C-terminus with an antigen, or a DNA expression vector comprising said nucleotide sequence, for use in vaccine prevention and therapy, wherein SEQ ID NO:1 is the following sequence:

MGCKWSKSSV VGWPAVRERM RRAEPAADGV GAASRDLEKH GAITSSNTAA TNADCAWLEA QEEEEVGFPV TPQVPLRPMT YKAAVDLSHF LKEKGGLEGL IHSQRRQDIL DLWIYHTQGY FPDWQNYPTG PGIRYPLTFG WCYKLVPVEP EKLEEANKGE NTSLLHPVSL HGMDDPGREV LEWRFDSRLA FHHVARELHP EYFKNC.

The nucleotide sequence or DNA expression vector according to the present invention can be administered preferably intramuscularly; other routes of administration can be aerosol administration (i.e. administration to the upper airway), intradermal, mucosal, sub-cute administration.

The antigen can be chosen from the group consisting of Human Papilloma virus antigen such as E6 and E7, HIV antigen such as Gag and Tat, Ebola virus antigen such as VP24, VP40, NP, and GP, West Nile virus antigen such as NS3, HBV antigen such as Core, HCV antigen such as Core, NS3, El and E2, Crimean-Congo virus antigen such as GP and NP, Influenza A virus antigen such as NP and M1, human melanoma antigen
such as MAGE-A3 and MART-1, human tumor-associated antigens such as Her2/Neu, Hox B7.

CLAIMS

1) Use of a~~A~~n expression vector comprising a polynucleotide encoding a fusion protein, said fusion protein comprising (i) human HIV-1 Nef protein with mutations 3C, 153L and 177G, fused at its C-terminus to (ii) an immunogenic antigen in the manufacture of a medicament for the prevention and treatment of disease in a patient, wherein such diseases are known to be mediated by CD8+ T cell response, wherein the medicament is to be administered by intramuscular injection into said patient; and optionally further comprises one or more pharmaceutically acceptable excipients and/or adjuvants.

2) The ~~expression vector~~use according to claim 1, said fusion protein consisting of (i) human HIV-1 Nef protein with mutations 3C, 153L and 177G, fused at its C-terminus to (ii) an immunogenic antigen.

3) The ~~expression vector~~use according to claim 1 or 2, wherein the antigen is chosen from the group consisting of Human Papilloma virus antigens ~~such as E6 and E7~~, HIV antigens ~~such as Gag and Tat~~, Ebola virus antigens ~~such as VP24, VP40, NP, and GP~~, West Nile virus antigens ~~such as NS3~~, HBV antigens ~~such as Core~~, HCV antigens ~~such as Core, NS3, E1 and E2~~, Crimean-Congo virus antigens ~~such as GP and NP~~, Influenza A virus antigens ~~such as NP and M1~~ , human melanoma antigens ~~such as MAGE-A3 and MART-1~~, and human tumor-associated antigens ~~such as Her2/Neu, Hox B7~~.

4) The use according to claim 3, wherein the Human Papilloma virus antigen is E6 or E7; wherein the HIV antigen is Gag or Tat; wherein the Ebola virus antigen is VP24, VP40, NP, or GP; wherein the West Nile virus antigen is NS3; wherein the HBV antigen is Core; wherein the HCV antigen is Core, NS3, E1 or E2; wherein the Crimean-Congo virus antigen is GP or NP; wherein the Influenza A virus antigen is NP or M1; wherein the human melanoma antigen is MAGE-A3 or MART-1; and wherein the human tumor-associated antigen is Her2/Neu or Hox B7.

5.) The u~~U~~se ~~of the expression vector~~ according to anyone of claims 1-3, ~~in the manufacture of a medicament for the prevention and~~wherein the ~~treatment of~~ disease~~s~~

to be treated is chosen from the group consisting of chronic infective diseases ~~such as HBV, HCV and HIV, tuberculosis and malaria~~, acute infective diseases ~~such as influenza, West Nile, Crimean-Congo hemorrhagic fever and Ebola diseases~~, and tumors ~~such as breast, pulmonary, prostate or bladder tumor, wherein the medicament is to be administered by intramuscular injection~~.

6.) The use according to claim 5, wherein the chronic infective diseases is HBV, HCV, HIV, tuberculosis or malaria; wherein the acute infective diseases is influenza, West Nile, Crimean-Congo hemorrhagic fever or Ebola diseases, and wherein the tumor is breast, pulmonary, prostate or bladder cancer.

7~~5~~) A v~~V~~accine composition for use as a vaccine for diseases known to be mediated by CD8+ T cell response, comprising ~~or consisting of~~ an expression vector comprising a polynucleotide encoding a fusion protein, said fusion protein comprising ~~or consisting of~~ (i) human HIV-1 Nef protein with mutations 3C, 153L and 177G, fused at its C-terminus to (ii) an immunogenic antigen, wherein the vaccine composition is to be administered by intramuscular injection; and optionally further comprises one or more pharmaceutically acceptable excipients and/or adjuvants.

8~~6~~) The v~~V~~accine composition according to claim ~~5~~7, wherein the antigen is chosen from the group consisting of Human Papilloma virus antigens ~~such as E6 and E7~~, HIV antigens ~~such as Gag and Tat~~, Ebola virus antigens ~~such as VP24, VP40, NP and GP~~, West Nile virus antigens ~~such as NS3~~, HBV antigens ~~such as Core~~, HCV antigens ~~such as Core, NS3, E1 and E2;~~, Crimean-Congo virus antigens ~~such as NP and GP;~~, Influenza A virus antigens ~~such as NP and M1 ;~~, human melanoma antigens ~~such as MAGE-A3 and MART-1 ;~~, and human tumor-associated antigens ~~such as Her2/Neu, HoxB7~~.

9~~7~~) The v~~V~~accine composition according to claim~~s~~ 8~~5 or 6~~, wherein the Human Papilloma virus antigen is E6 or E7; wherein the HIV antigen is Gag or Tat; wherein the Ebola virus antigen is VP24, VP40, NP, or GP; wherein the West Nile virus antigen is NS3; wherein the HBV antigen is Core; wherein the HCV antigen is Core, NS3, E1 or E2; wherein the Crimean-Congo virus antigen is GP or NP; wherein the Influenza A virus antigen is NP or M1; wherein the human melanoma antigen is MAGE-A3 or

MART-1; and wherein the human tumor-associated antigen is Her2/Neu or Hox B7~~wherein the vaccine composition is in a form suitable for a route of intramuscular administration~~.

~~8~~10) The v~~V~~accine composition according to anyone of claims ~~5-7~~7-9, wherein the adjuvant is an adjuvant of CD8+ T cells response.

~~9) Vaccine composition according to claims 7 or 8, for use as a vaccine.~~

~~10~~11) A u~~U~~se of the vaccine composition according to any one of claims 6~~5~~-10~~9~~ in the manufacture of a medicament for the prevention and treatment of a disease~~s~~ chosen from the group consisting of chronic infective diseases ~~such as HBV, HCV and HIV, tuberculosis and malaria~~, acute infective diseases ~~such as influenza, West Nile, Crimean-Congo hemorrhagic fever and Ebola diseases~~, and tumors ~~such as breast, pulmonary, prostate or bladder tumor~~, wherein such diseases are known to be mediated by CD8+ T cell response, and wherein the medicament is to be administered by intramuscular injection.

12) The use according to claim 11, wherein the chronic infective diseases is HBV, HCV, HIV, tuberculosis or malaria; wherein the acute infective diseases is influenza, West Nile, Crimean-Congo hemorrhagic fever or Ebola diseases, and wherein the tumor is breast, pulmonary, prostate or bladder cancer.

~~11~~13) The expression vector comprising a polynucleotide encoding a fusion protein, said fusion protein comprising (i) human HIV-1 Nef protein with mutations 3C, 153L and 177G, fused at its C-terminus to (ii) an immunogenic antigen ~~according to any one of claims 1-3~~ for use as a vaccine for diseases known to be mediated by CD8+ T cell response, wherein the expression vector is ~~in a form suitable for administration~~ to be administered by intramuscular injection.