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

Summary

In one aspect, there is provided 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 immunogenic antigen, or a DNA expression vector comprising said nucleotide sequence, for use in vaccine prevention and therapy by inducing a CTL immune response, 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.

In another aspect, there is provided a use of the nucleotide sequence or DNA 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.

In another aspect, there is provided a pharmaceutical composition, that is immunogenic, comprising or consisting of 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, in association with one or more pharmaceutically acceptable excipients and/or adjuvants, 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.

In another aspect, there is provided a use of the pharmaceutical composition as described herein 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.

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.

As mentioned above, the nucleotide sequence expressing the exosome-anchoring protein of sequence SEQ ID NO:1 can be the following nucleotide sequence SEQ ID NO:2 (Nef^{mut} nucleotide sequence):

atg ggt tgc aag tgg tca aaa agt agt gtg gtt gga tgg cct gct gta agg gaa aga
atg aga cga gct gag cca gca gca gat ggg gtg gga gca gca tct cga gac cta
gaa aaa cat gga gca atc aca agt agc aat aca gca gct acc aat gct gat tgt
gcc tgg cta gaa gca caa gag gag gag gag gtg ggt ttt cca gtc aca cct cag

CLAIMS

1) 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 immunogenic antigen, or a DNA expression vector comprising said nucleotide sequence, for use in vaccine prevention and therapy by inducing a CTL immune response, 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.

2) Nucleotide sequence or DNA expression vector according to claim 1, for use according to claim 1, wherein said nucleotide sequence or DNA expression vector is to be administered by intramuscular administration.

3) Nucleotide sequence or DNA expression vector according to anyone of claims 1-2, for use according to anyone of claims 1-2, wherein the antigen is 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, E1 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.

4) Nucleotide sequence or DNA expression vector according to anyone of claims 1-3, for use according to anyone of claims 1-3, wherein the nucleotide sequence expressing the exosome-anchoring protein of sequence SEQ ID NO:1 is the following nucleotide sequence SEQ ID NO:2:

atg ggt tgc aag tgg tca aaa agt agt gtg gtt gga tgg cct gct gta agg gaa aga atg aga cga gct gag cca gca gca gat ggg gtg gga gca gca tct cga gac cta gaa aaa cat gga gca atc aca agt agc aat aca gca gct acc aat gct gat tgt gcc tgg cta gaa gca caa gag gag gag gag gtg ggt ttt cca gtc aca cct cag gta cct tta aga cca atg act tac aag gca gct gta gat ctt agc cac ttt tta aaa gaa aag ggg gga ctg gaa ggg cta att cac tcc caa cga aga caa gat atc ctt gat ctg tgg atc tac cac aca caa ggc tac ttc cct gat tgg cag aac tac aca cca gga cca ggg gtt aga tat cca ctg acc ttt gga tgg tgc tac aag cta gta cca gtt gag cca gag aag tta gaa gaa gcc aac aaa gga gag aac acc agc ttg tta cac cct gtg agc ctg cat gga atg gat gac ccg gcg aga gaa gtg tta gag tgg agg ttt gac agc cgc cta gca ttt cat cac gtg gcc cga gag ctg cat ccg gag tac ttc aag aac tgc tga

5) Use of the nucleotide sequence or DNA expression vector according to anyone of claims 1-4, 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.

6) Pharmaceutical composition, that is immunogenic, comprising or consisting of 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, in association with one or more pharmaceutically acceptable excipients and/or adjuvants, 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.

7) Pharmaceutical composition according to claim 6, wherein the antigen is 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, E1 and E2; Crimean-Congo virus antigen such as NP and GP; 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, HoxB7.

8) Pharmaceutical composition according to anyone of claims 6-7, wherein the nucleotide sequence expressing the exosome-anchoring protein of sequence SEQ ID NO:1 is the following sequence SEQ ID NO:2:

atg ggt tgc aag tgg tca aaa agt agt gtg gtt gga tgg cct gct gta agg gaa aga atg aga cga gct gag cca gca gca gat ggg gtg gga gca gca tct cga gac cta gaa aaa cat gga gca atc aca agt agc aat aca gca gct acc aat gct gat tgt gcc tgg cta gaa gca caa gag gag gag gag gtg ggt ttt cca gtc aca cct cag gta cct tta aga cca atg act tac aag gca gct gta gat ctt agc cac ttt tta aaa gaa aag ggg gga ctg gaa ggg cta att cac tcc caa cga aga caa gat atc ctt gat ctg tgg atc tac cac aca caa ggc tac ttc cct gat tgg cag aac tac aca cca gga cca ggg gtt aga tat cca ctg acc ttt gga tgg tgc tac aag cta gta cca gtt gag cca gag aag tta gaa gaa gcc aac aaa gga gag aac acc age ttg tta cac cct gtg agc ctg cat gga atg gat gac ccg gcg aga gaa gtg tta gag tgg agg ttt gac agc cgc cta gca ttt cat cac gtg gcc cga gag ctg cat ccg gag tac ttc aag aac tgc tga

9) Pharmaceutical composition according to anyone of claims 6-8, wherein the pharmaceutical composition is in a form suitable for a route of intramuscular administration.

10) Pharmaceutical composition according to anyone of claims 6-9, wherein the adjuvant is an adjuvant of CD8+ T cells response.

11) Pharmaceutical composition according to anyone of claims 6-10, for use in vaccine prevention and therapy.

12) Use of the pharmaceutical composition according to any one of claims 6-10 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.