active fragment of MPHOSPH1 (SEQ ID NO: 126). Such peptides can be used to induce CTLs in vitro or ex vivo, or to be administered directly to a subject so as to induce in vivo immune responses against cancers, examples of which include, but are not limited to, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, CML, colorectal cancer, gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal cancer and soft tissue tumor.

[0011a] In one aspect, there is provided an isolated peptide of the following (a) or (b):

(a) a peptide consisting of the amino acid sequence of SEQ ID NO:120;

(b) a peptide consisting of an amino acid sequence that 1 or 2 amino acid(s) are substituted, in the amino acid sequence of SEQ ID NO:120, and wherein the peptide has cytotoxic T lymphocyte (CTL) inducibility.

[0012] The peptides of the present ~~invention~~disclosure are generally less than 15, 14, 13, 12, 11, or 10 amino acids in length. ~~Preferred~~ Examplary peptides of the present ~~invention are~~disclosure include nonapeptides or decapeptides. ~~Particularly preferred~~Examplary peptides have an amino acid sequence selected from among SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120, since those peptides demonstrated to bind to the HLA-A2 antigen and induce CTL.

[0013] ~~Thus, i~~In some ~~embodiments~~examples, the peptides of the present invention are peptides of less than 15, 14, 13, 12, 11, or 10 amino acids in length that have an amino acid sequence selected from among SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120. In typical ~~embodiments~~examples, the peptides of the present invention are nonapeptides or decapeptides having an amino acid sequence selected from among SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120. Furthermore, as demonstrated herein, a peptide having the amino acid sequence of SEQ ID NO: 120 was confirmed to induce CTLs targeting tumor cells expressing the MPHOSPH1 and HLA-A2 antigen. Thus, in preferred ~~embodiments~~examples, the peptides of the present invention are peptides having an amino acid sequence of SEQ ID NO: 120.

[0014] When contacted with antigen presenting cells (APCs) in vitro, ex vivo or in vivo, the peptides of the present invention will bind with HLA-A2 antigens on APCs and be presented on APCs as complexes with HLA-A2 antigens. Alternatively, the peptides of the present invention may be taken into by APCs, processed to fragments composed of an amino acid sequence selected from among SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120 in APCs, and presented on APCs as complexes with HLA-A2 antigens. Consequently, CTLs specific to such peptides are induced and such CTLs are considered to be as elements of the present invention.

[0015] The present ~~invention~~disclosure also contemplates modified peptides having an amino acid sequence in which one, two or several amino acids are substituted, deleted, inserted and/or added in the amino acid sequence selected from among SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120, so long as the modified peptides retain the CTL inducibility equivalent to that of the original unmodified peptide. To that end, the present ~~invention~~disclosure provides an isolated peptide of less than 15, 14, 13, 12, 11, or 10 amino acids in length, which has CTL inducibility and comprises the amino acid sequence selected from the group consisting of:

(i) an amino acid sequence that 1, 2, or several amino acid(s) are substituted in the

amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14 and 64, and

(ii) the amino acid sequence of (i), wherein the amino acid sequence has one or both of the following characteristics:

(a) the second amino acid from the N-terminus of said SEQ ID NO is selected from the group consisting of leucine and methionine; and

(b) the C-terminal amino acid of said SEQ ID NO is selected from the group consisting of valine and leucine.

[0016] Moreover, the present ~~invention~~disclosure also provides an isolated peptide of less than 15, 14, 13, 12, or 11 amino acids in length, which has CTL inducibility and comprises the amino acid sequence selected from the group consisting of:

(i') an amino acid sequence that 1, 2, or several amino acid(s) are substituted in the amino acid sequence selected from the group consisting of SEQ ID NOs: 73, 77, 79, 97, 103 and 120, and

(ii') the amino acid sequence of (i'), wherein the amino acid sequence has one or both of the following characteristics:

(a) the second amino acid from the N-terminus of said SEQ ID NO is selected from the group consisting of leucine and methionine; and

(b) the C-terminal amino acid of said SEQ ID NO is selected from the group consisting of valine and leucine.

[0017] As demonstrated herein, such peptides may bind with HLA-A2 antigens on APCs and be presented on APCs as complexes with HLA-A2 antigens. Alternatively, such peptides may be taken into by APCs, processed to fragments composed of an amino acid sequence selected from among (i), (ii), (i'), and (ii') in APCs, and presented on APCs as complexes with HLA-A2 antigens, when those peptides are contacted with APCs. Consequently, CTLs specific to such peptides are induced and such CTLs are considered to be as elements of the present ~~invention~~disclosure.

The present invention further encompasses isolated polynucleotides that encode any of the peptides of the present invention. Thus, in one aspect, there is provided an isolated polynucleotide encoding the peptide of the present invention. These polynucleotides can be used to induce or prepare APCs having CTL inducibility. Like above-described peptides of the present invention, such APCs can be administered to a subject for inducing immune responses against cancers.

[0018] When administered to a subject, the peptides of the present invention are presented on the surface of APCs so as to induce CTLs targeting the respective peptides. Therefore, one object of the present invention is to provide agents or compositions that include one or more peptide(s) or polynucleotide(s) provided by the present invention for inducing either or both of APCs and CTLs. Such agents or compositions can be also used for one or more purpose(s) selected from among the treatment of cancer, the

prophylaxis of cancer, and the prevention of postoperative recurrence of cancer. Examples of targetted cancers include, but are not limited to, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, CML, colorectal cancer, gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal cancer and soft tissue tumor. Thus, it is yet another object of the present invention to provide pharmaceutical agents or compositions for either or both of the treatment of cancer and the prophylaxis of cancer, such pharmaceutical agents or compositions formulated to include one or more peptides or polynucleotides of the present invention. Instead of or in addition to the peptides or polynucleotides of the present invention, the pharmaceutical agents or compositions of the present invention may include as active ingredients APCs or exosomes that present any of the peptides of the present invention.

[0018a] Thus in one aspect, there is provided a composition for inducing a CTL, wherein the composition comprises one or more peptide(s) of the present invention, or one or more polynucleotide(s) of the present invention. In another aspect, there is provided a composition for inducing an APC having CTL inducibility, wherein the composition comprises one or more peptide(s) of the present invention, or one or more polynucleotide(s) of the present invention. In yet another aspect, there is provided a pharmaceutical composition comprising at least one active ingredient selected from the group consisting of:

(a) one or more peptides of the present invention;

(b) one or more polynucleotides encoding the peptide of the present invention;

(c) one or more APCs that present a complex of the peptide of the present invention and an HLA antigen on their surface;

(d) one or more exosomes that present a complex of the peptide of the present invention and an HLA antigen on their surface; and

(e) one or more CTLs that recognize a cell presenting a complex of the peptide of the present invention and an HLA antigen on its surface.

[0019] The peptides or polynucleotides of the present invention may be used to induce APCs that present on the surface a complex of an HLA antigen and a present peptide, for example, by contacting APCs with the peptide of the present invention or introducing a polynucleotide encoding a peptide of the present invention into APCs. Such APCs have the ability of inducing CTLs that specifically recognize cells that presents target peptides on their surface and find use in cancer immunotherapy. Accordingly, the present invention encompasses the methods for inducing APCs having

CTL inducibilitiy as well as the APCs obtained by such methods. Thus, in one aspect, there is provided an *ex vivo* or *in vitro* method for inducing an antigen-presenting cell (APC) having CTL inducibility, said method comprising a step selected from the group consisting of :

(a) contacting an APC with the peptide of the present invention *in vitro* or *ex vivo*, and

(b) introducing a polynucleotide encoding the peptide of the present invention into an APC.

In addition, the invention present ~~inventiondisclosure~~ also encompasses the agents or compositions for use in inducing APCs, such agents or compositions including any peptides or polynucleotides of the present invention.

[0020] It is further object of the present invention to provide a method for inducing CTLs, such method including the step of co-culturing CD8 positive T cells with APCs or exosomes presenting the peptide of the present invention on its surface or the step of introducing a polynucleotide encoding both of T cell receptor (TCR) subunits or polynucleotides encoding each of TCR subunits, wherein the TCR can binds to a complex of the peptide of the present invention and HLA antigen presented on cell surface. Thus, in one aspect there is provided an *ex vivo* or *in vitro* method for inducing CTL, said method comprising a step selected from the group consisting of:

(a) co-culturing a CD8 positive T cell with an APC that presents on its surface a complex of an HLA antigen and the peptide of the present invention;

(b) co-culturing a CD8 positive T cell with an exosome that presents on its surface a complex of an HLA antigen and the peptide of the present invention; and

(c) introducing a polynucleotide encoding both of T cell receptor (TCR) subunits or polynucleotides encoding each of TCR subunits into a CD8 positive T cell, wherein the TCR can bind to a complex of an HLA antigen and the peptide of any of the present invention presented on a cell surface.

CTLs obtained by such methods can find use in either or both of the treatment of cancer and the prevention of cancer. Examples of cancers include, but are not limited to, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, CML, colorectal cancer, gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal cancer and soft tissue tumor.

[0021] Yet another ~~objectaspect~~ of the present invention is to provide isolated APCs that present on the surface a complex of an HLA antigen and a peptide of the present invention. The present invention further provides isolated CTLs that target peptides of the present invention. Thus in another aspect , there is provided an isolated CTL that recognizes a cell presenting on its surface a complex of an HLA antigen and the peptide of the present invention. These APCs and CTLs find utility in the context of cancer immunotheraphy. ~~It is yet another object of the present invention to provide~~ The present disclosure also provides methods for inducing an

immune response against a cancer in a subject in need thereof, such methods including the step of administering an agent or composition that include at least one component selected from among the peptides of the present invention, polynucleotides encoding such peptides, exosomes or APCs presenting such peptides and CTLs that recognize cells presenting such peptides on their surface.

[0022] The applicability of the present invention extends to any of a number of the diseases relating to or arising from MPHOSPH1 over-expression, such as cancer, examples of which include, but are not limited to, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, CML, colorectal cancer, gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal cancer and soft tissue tumor.

[0022a] In one aspect, there is provided an isolated antibody or immunologically active fragment thereof against the peptide of the present invention. In another aspect, there is provided a vector comprising a nucleotide sequence encoding the peptide of the present invention. In another aspect there is provided a host cell transformed or transfected with the vector of the present invention. In yet another aspect, there is provided a diagnostic kit comprising the peptide of the present invention, the polynucleotide of the present invention or the antibody of the present invention.

[0023] ~~More specifically, t~~The present ~~invention~~disclosure also provides followings:

[1] An isolated peptide of the following (a) or (b):

(a) a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120;

(b) a peptide comprising an amino acid sequence that 1, 2, or several amino acid(s) are substituted, deleted, inserted, and/or added in the amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120, and wherein the peptide has cytotoxic T lymphocyte (CTL) inducibility,

[2] The isolated peptide of [1], wherein the peptide has one or both of the following characteristics:

(a) the second amino acid from the N-terminus of the amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120 is selected from the group consisting of leucine and methionine; and

(b) the C-terminal amino acid of the amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120 is selected from the group consisting of valine and leucine,

[3] The isolated peptide of [1] or [2], wherein the peptide is a nonapeptide or decapeptide,

[4] An isolated polynucleotide encoding the peptide of any one of [1] to [3],

[5] A composition for inducing a CTL, wherein the composition comprises one or more peptide(s) of any one of [1] to [3], or one or more polynucleotide(s) of [4],

[6] A composition for inducing an APC having CTL inducibility, wherein the composition comprises one or more peptide(s) of any one of [1] to [3], or one or more polynucleotide(s) of [4],

[7] A pharmaceutical composition comprising at least one active ingredient selected from the group consisting of:

(a) one or more peptides of any one of [1] to [3];

(b) one or more polynucleotides encoding the peptide of any one of [1] to [3];

Claims

[Claim 1] An isolated peptide of the following (a) or (b):
(a) a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120;
(b) a peptide comprising an amino acid sequence that 1, 2, or several amino acid(s) are substituted, deleted, inserted, and/or added in the amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120, and wherein the peptide has cytotoxic T lymphocyte (CTL) inducibility.

[Claim 2] The isolated peptide of claim 1, wherein the peptide has one or both of the following characteristics:
(a) the second amino acid from the N-terminus of the amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120 is selected from the group consisting of leucine and methionine; and
(b) the C-terminal amino acid of the amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 14, 64, 73, 77, 79, 97, 103 and 120 is selected from the group consisting of valine and leucine.

[Claim 3] The isolated peptide of claim 1 or 2, wherein the peptide is a nonapeptide or decapeptide.

[Claim 4] An isolated polynucleotide encoding the peptide of any one of claim 1 to 3.

[Claim 5] A composition for inducing a CTL, wherein the composition comprises one or more peptide(s) of any one of claims 1 to 3, or one or more polynucleotide(s) of claim 4,

[Claim 6] A composition for inducing an APC having CTL inducibility, wherein the composition comprises one or more peptide(s) of any one of claims 1 to 3, or one or more polynucleotide(s) of claim 4.

[Claim 7] A pharmaceutical composition comprising at least one active ingredient selected from the group consisting of:
(a) one or more peptides of any one of claims 1 to 3;
(b) one or more polynucleotides encoding the peptide of any one of claims 1 to 3;
(c) one or more APCs or exosomes that present a complex of the peptide of any one of claims 1 to 3 and an HLA antigen on their surface; and

(d) one or more CTLs that recognize a cell presenting a complex of the peptide of any one of claims 1 to 3 and an HLA antigen on its surface.

[Claim 8] The pharmaceutical composition of claim 7 for use in either or both of the treatment and the prophylaxis of cancer, or inducing an immune response against cancer in a subject.

[Claim 9] The pharmaceutical composition of claim 7 or 8, wherein the pharmaceutical composition is formulated for administration to a subject whose HLA antigen is HLA-A2.

[Claim 10] A method for inducing an antigen-presenting cell (APC) having CTL inducibility, said method comprising a step selected from the group consisting of:

(a) contacting an APC with the peptide of any one of claims 1 to 3 in vitro, ex vivo or in vivo, and

(b) introducing a polynucleotide encoding the peptide of any one of claims 1 to 3 into an APC.

[Claim 11] A method for inducing a CTL, said method comprising a step selected from the group consisting of:

(a) co-culturing a CD8 positive T cell with an APC that presents on its surface a complex of an HLA antigen and the peptide of any one of claims 1 to 3;

(b) co-culturing a CD8 positive T cell with an exosome that presents on its surface a complex of an HLA antigen and the peptide of any one of claim 1 to 3; and

(c) introducing a polynucleotide encoding both of T cell receptor (TCR) subunits or polynucleotides encoding each of TCR subunits into a CD8 positive T cell, wherein the TCR can bind to a complex of an HLA antigen and the peptide of any one of claims 1 to 3 presented on a cell surface.

[Claim 12] An isolated APC that presents on its surface a complex of an HLA antigen and the peptide of any one of claims 1 to 3.

[Claim 13] The APC of claim 12, which is induced by the method of claim 10.

[Claim 14] An isolated CTL that recognizes a cell presenting on its surface a complex of an HLA antigen and the peptide of any one of claims 1 to 3.

[Claim 15] The CTL of claim 14, wherein said CTL is induced by the method of claim 11.

[Claim 16] A method of either or both of the treatment and prophylaxis of cancer in a subject, wherein the method comprises the step of administering to the subject (a) pharmaceutically effective amount(s) of:

(a) one or more peptides of any one of claims 1 to 3;
(b) one or more polynucleotides encoding the peptide of any one of claims 1 to 3;
(c) one or more APCs or exosomes that present a complex of the peptide of any one of claims 1 to 3 and an HLA antigen on their surface; or
(d) one or more CTLs that recognize a cell presenting a complex of the peptide of any one of claims 1 to 3 and an HLA antigen on its surface.

[Claim 17] A method of inducing an immune response against cancer in a subject in need thereof, said method comprising the step of administering to the subject a composition comprising a peptide of any one of claims 1 to 3 or a polynucleotide encoding the peptide.

[Claim 18] An antibody or immunologically active fragment thereof against the peptide of any one of claims 1 to 3.

[Claim 19] A vector comprising a nucleotide sequence encoding the peptide of any one of claims 1 to 3.

[Claim 20] A host cell transformed or transfected with the vector of claim 19.

[Claim 21] A diagnostic kit comprising the peptide of any one of claims 1 to 3, the polynucleotide of claim 4 or the antibody of claim 18.

Claims

1. An isolated peptide of the following (a) or (b):
   (a) a peptide consisting of the amino acid sequence of SEQ ID NO:120;
   (b) a peptide consisting of an amino acid sequence that 1 or 2 amino acid(s) are substituted, in the amino acid sequence of SEQ ID NO:120, and wherein the peptide has cytotoxic T lymphocyte (CTL) inducibility.

2. The isolated peptide of Claim 1, wherein the peptide has one or both of the following characteristics:
   (a) the second amino acid from the N-terminus of the amino acid sequence of SEQ ID NO:120 is substituted with amino acid selected from the group consisting of leucine and methionine; and
   (b) the C-terminal amino acid of the amino acid sequence of SEQ ID NO:120 is substituted with amino acid selected from the group consisting of valine and leucine.

3. The isolated peptide of Claim 1, wherein the peptide consists of the amino acid sequence of SEQ ID NO:120.

4. An isolated polynucleotide encoding the peptide of any one of Claims 1 to 3.

5. A composition for inducing a CTL, wherein the composition comprises one or more peptide(s) of any one of Claims 1 to 3, or one or more polynucleotide(s) of Claim 4.

6. A composition for inducing an APC having CTL inducibility, wherein the composition comprises one or more peptide(s) of any one of Claims 1 to 3, or one or more polynucleotide(s) of Claim 4.

7. A pharmaceutical composition comprising at least one active ingredient selected from the group consisting of:
   (a) one or more peptides of any one of Claims 1 to 3;
   (b) one or more polynucleotides encoding the peptide of any one of Claims 1 to 3;
   (c) one or more APCs that present a complex of the peptide of any one of Claims 1 to 3 and an HLA antigen on their surface;
   (d) one or more exosomes that present a complex of the peptide of any one of Claims 1 to 3 and an HLA antigen on their surface; and
   (e) one or more CTLs that recognize a cell presenting a complex of the peptide of any one of Claims 1 to 3 and an HLA antigen on its surface.

8. The pharmaceutical composition of Claim 7 for use in either or both of the treatment and the prophylaxis of cancer, or inducing an immune response against cancer in a subject.

9. The pharmaceutical composition of Claim 7 or 8, wherein the pharmaceutical composition is formulated for administration to a subject whose HLA antigen is HLA-A2.

10. An *ex vivo* or *in vitro* method for inducing an antigen-presenting cell (APC) having CTL inducibility, said method comprising a step selected from the group consisting of:

    (a) contacting an APC with the peptide of any one of Claims 1 to 3 *in vitro* or *ex vivo*, and

    (b) introducing a polynucleotide encoding the peptide of any one of Claims 1 to 3 into an APC.

11. An *ex vivo* or *in vitro* method for inducing a CTL, said method comprising a step selected from the group consisting of:

    (a) co-culturing a CD8 positive T cell with an APC that presents on its surface a complex of an HLA antigen and the peptide of any one of Claims 1 to 3;

    (b) co-culturing a CD8 positive T cell with an exosome that presents on its surface a complex of an HLA antigen and the peptide of any one of Claim 1 to 3; and

    (c) introducing a polynucleotide encoding both of T cell receptor (TCR) subunits or polynucleotides encoding each of TCR subunits into a CD8 positive T cell, wherein the TCR can bind to a complex of an HLA antigen and the peptide of any one of Claims 1 to 3 presented on a cell surface.

12. An isolated APC that presents on its surface a complex of an HLA antigen and the peptide of any one of Claims 1 to 3.

13. The APC of Claim 12, which is induced by the method of Claim 10.

14. An isolated CTL that recognizes a cell presenting on its surface a complex of an HLA antigen and the peptide of any one of Claims 1 to 3.

15. The CTL of Claim 14, wherein said CTL is induced by the method of Claim 11.

16. An isolated antibody or immunologically active fragment thereof against the peptide of any one of Claims 1 to 3.

17. A vector comprising a nucleotide sequence encoding the peptide of any one of Claims 1 to 3.

18. A host cell transformed or transfected with the vector of Claim 17.

19. A diagnostic kit comprising the peptide of any one of Claims 1 to 3, the polynucleotide of Claim 4 or the antibody of Claim 16.