carcinoma, hepatocellular carcinoma, leukemia, colorectal cancer and melanoma (NPL 16-19). Recent studies indicating that kinase activity plays an important role in breast carcinogenesis has renewed research interest in cancer-linked kinases such as TOPK. To that end, Northern blot analysis has revealed that TOPK transcript is highly expressed in breast cancer cells but is hardly detectable in normal human tissues except testis. In addition, knockdown of endogenous TOPK expression by siRNA in breast cancer cell lines has been shown to attenuate the cytokinesis and lead to apoptosis of the cancer cells (NPL 20).

[Citation List]

[Non Patent Literature]

[0006]

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Summary

[0007]

The present disclosure is based, at least in part, on the discovery of novel peptides that may serve as suitable targets of immunotherapy. Because TAAs are generally perceived by the immune system as "self" and therefore often have no innate immunogenicity, the discovery of appropriate targets is of extreme importance. Through the present disclosure, TOPK (SEQ ID NO: 86 encoded by the gene of GenBank Accession No. NM_018492 (SEQ ID NO: 85)) is demonstrated to be specifically over-expressed

in cancer cells, in particular acute myeloid leukemia (AML), bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, colorectal cancer, diffuse-type gastric cancer, non-small cell lung cancer (NSCLC), lymphoma, osteosarcoma, prostate cancer, renal carcinoma, small cell lung cancer (SCLC) and soft tissue tumor, but not limited thereto. Thus, the present disclosure focuses on TOPK as an appropriate candidate target of cancer/tumor immunotherapy.

[0007a] In one aspect, the present disclosure refers to an isolated peptide of less than 15 amino acids selected from the group consisting of (a) and (b) below: (a) an isolated peptide having cytotoxic T lymphocyte (CTL) inducibility comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76, and (b) an isolated peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76, in which 1 or 2 amino acid(s) are substituted, inserted, and/or added, wherein the peptide has CTL inducibility.

[0007b] In another aspect, the present disclosure refers to an isolated peptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76.

[0007c] In yet another aspect, the present disclosure refers to an isolated polynucleotide encoding the isolated peptide as disclosed herein.

[0007d] In yet another aspect, the present disclosure refers to a composition for inducing a CTL, wherein the composition comprises one or more peptide(s) as disclosed herein, or one or more polynucleotide(s) as disclosed herein.

[0007e] In yet another aspect, the present disclosure refers to a pharmaceutical composition comprising: (a) one or more peptide(s) as disclosed herein; (b) one or more polynucleotide(s) as disclosed herein; (c) one or more APC(s) that present a complex of the peptide as disclosed herein and an HLA antigen on their surface; (d) one or more exosome(s) that present a complex of the peptide as disclosed herein and an HLA antigen on their surface; or (e) one or more CTL(s) that can recognize a cell presenting a complex of the peptide as disclosed herein and an HLA antigen on their surface, in combination with a pharmaceutically acceptable carrier, wherein the pharmaceutical composition is formulated for the treatment and/or prophylaxis of cancer, the prevention of a postoperative recurrence thereof, and/or the induction of an immune response against cancer

[0007f] In yet another aspect, the present disclosure refers to an *in vitro* method for inducing an antigen-presenting cell (APC) with CTL inducibility, said method comprising the step selected from the group consisting of: (a) contacting an APC with the peptide as disclosed herein *in vitro*, and (b) introducing a polynucleotide encoding the peptide as disclosed herein into an APC.

[0007g] In yet another aspect, the present disclosure refers to an *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 as disclosed herein, (b) co-culturing a CD8-positive T cells with an exosome that presents on its surface a complex of an HLA antigen and the peptide as disclosed herein, and (c) introducing into a CD8-positive T cell a polynucleotide/polynucleotides encoding a T cell receptor (TCR) subunit polypeptides, wherein the TCR formed by said TCR subunit polypeptides is capable of

binding to a complex of an HLA antigen and the peptide as disclosed herein on a cell surface.
[0007h] In yet another aspect, the present disclosure refers to an isolated APC that presents on its surface a complex of an HLA antigen and the peptide as disclosed herein.
[0007i] In yet another aspect, the present disclosure refers to an isolated CTL that targets the peptide as disclosed herein.
[0007j] In yet another aspect, the present disclosure refers to a composition for use in inducing an immune response against cancer in a subject in need thereof, wherein the composition comprises the peptide as disclosed herein or a polynucleotide encoding the peptide.
[0007k] In yet another aspect, the present disclosure refers to a use of a composition comprising the peptide as disclosed herein or a polynucleotide encoding the peptide in the manufacture of a medicament for treating cancer by inducing an immune response against cancer in a subject in need thereof.
[0007l] In yet another aspect, the present disclosure refers to a vector comprising a nucleotide sequence encoding the peptide as disclosed herein.
[0007m] In yet another aspect, the present disclosure refers to a host cell transformed or transfected with the vector as disclosed herein.
[0007n] In yet another aspect, the present disclosure refers to a diagnostic kit comprising the peptide as disclosed herein or the polynucleotide as disclosed herein.
[0007o] In yet another aspect, the present disclosure refers to a method of screening for a peptide having an ability to induce a CTL that has specific cytotoxic activity against a cell that presents a fragment derived from TOPK, wherein the method comprises the steps of: (i) providing a candidate sequence consisting of an amino acid sequence modified by substituting, inserting and/or adding one or two amino acid residues to an original amino acid sequence, wherein the original amino acid sequence is selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76; (ii) selecting a candidate sequence that does not have substantial significant homology with the peptides derived from any known human gene products other than TOPK; (iii) contacting a peptide consisting of the candidate sequence selected in step (ii) with an antigen presenting cell; (iv) contacting the antigen presenting cell of step (iii) with a CD8-positive T cell; and (v) identifying the peptide of which CTL inducibility is same to or higher than a peptide consisting of the original amino acid sequence.
[0008]
To that end, the present disclosure is directed, at least in part, to the identification of specific epitope peptides among the gene products of TOPK that possess the ability to induce cytotoxic T lymphocytes (CTLs) specific to TOPK. As discussed in greater detail below, peripheral blood mononuclear cells (PBMCs) obtained from a healthy donor were stimulated using HLA (human leukocyte antigen)-A*2402 or HLA-A*0201 binding candidate peptides derived from TOPK. CTL lines were then established with specific cytotoxicity against the HLA-A24 or HLA-A2 positive target cells pulsed with each of candidate peptides. The results herein demonstrate that these peptides are HLA-A24 or HLA-A2 restricted epitope peptides that can induce potent and specific immune responses against cells expressing TOPK. These results further indicate that TOPK is strongly immunogenic and that the epitopes thereof are effective targets for tumor immunotherapy.

[0009]
Accordingly, it is an object of the present disclosure is to provide isolated peptides that have an ability to bind an HLA antigen and include the TOPK sequence (SEQ ID NO: 86) or an immunogenically active fragment thereof. These peptides are expected to have CTL inducibility and, thus, can be used to induce a CTL in vitro, ex vivo or in 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, AML, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, colorectal cancer, diffuse-type gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal carcinoma, SCLC and soft tissue tumor.
[0010]
Preferred peptides are nonapeptides and decapeptides, and more preferably nonapeptides and decapeptides having an amino acid sequence selected from among SEQ ID NOs: 2 to 40 and 42 to 84. Of these, the peptides having an amino sequence selected from among SEQ ID NOs: 2, 3, 6, 27, 28, 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76 are most preferred.
[0011]
The present disclosure also contemplates modified peptides having an amino acid sequence selected from among SEQ ID NOs: 2 to 40 and 42 to 84 in which one, two or more amino acids are substituted, deleted, inserted and/or added, provided the resulting modified peptides retain the requisite CTL inducibility of the original unmodified peptide.
[0012]
The present disclosure further encompasses isolated polynucleotides encoding any

one of peptides of the present disclosure. These polynucleotides can be used to induce or prepare antigen-presenting cells (APCs) having CTL inducibility. Like the above-described peptides of the present disclosure, such APCs can be administered to a subject for inducing immune responses against cancers.

[0013]

When administered to a subject, the peptides of the present disclosure are preferably presented on the surface of APCs so as to induce CTLs targeting the respective peptides. Therefore, one object of the present disclosure is to provide agents or compositions for inducing a CTL, such compositions or agents including one or more peptides of the present disclosure, or one or more polynucleotides encoding such peptides. Such agents or compositions can be used for the treatment and/or prophylaxis of a primary cancer, a metastasis or post-operative recurrence thereof. Examples of targeted cancers contemplated by the present disclosure include, but are not limited to, AML, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, colorectal cancer, diffuse-type gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal carcinoma, SCLC and soft tissue tumor.

[0014]

The present disclosure further contemplates pharmaceutical compositions or agents that include one or more peptides or one or more polynucleotides of the present disclosure formulated for the treatment and/or prophylaxis of a primary cancer, metastasis or postoperative recurrence cancer as noted above. Instead of or in addition to the present peptides or polynucleotides, the present pharmaceutical agents or compositions may include as active ingredients APCs and/or exosomes that present any of the peptides of the present disclosure.

[0015]

The peptides or polynucleotides of the present disclosure may be used to induce APCs that present on the surface a complex of an HLA antigen and a peptide of the present disclosure, for example, by contacting APCs derived from a subject with the peptide of the present disclosure or introducing a polynucleotide encoding the peptide of the present invention into APCs. Such APCs have high CTL inducibility against target peptides and are useful for cancer immunotherapy. Accordingly, the present disclosure encompasses the methods for inducing APCs with CTL inducibility as well as the APCs obtained by the methods.

[0016]

It is a further object of the present disclosure to provide methods for inducing CTLs, such methods including the step of co-culturing CD8-positive T cells with APCs presenting on its surface a complex of an HLA antigen and the peptide of the present disclosure, the step of co-culturing CD8-positive T cells with exosomes presenting on its surface a complex of an HLA antigen and the peptide of the present disclosure, or the step of introducing a polynucleotide/polynucleotides coding for T cell receptor (TCR) subunit polypeptides wherein the TCR formed by the subunit polypeptides can bind to a peptide of the present disclosure. CTLs obtained by such methods find use in

the treatment and/or prevention of cancers, more particularly AML, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, colorectal cancer, diffuse-type gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal carcinoma, SCLC and soft tissue tumor. Accordingly, the present invention encompasses the methods for inducing CTLs as well as the CTLs obtained by the methods. Yet another object of the present disclosure is to provide isolated APCs that present on the surface a complex of an HLA antigen and a peptide of the present disclosure. The present disclosure further provides isolated CTLs that target peptides of the present disclosure. These APCs and CTLs may be used for cancer immunotherapy.

[0017]

It is yet another object of the present disclosure to provide methods for inducing an immune response against a cancer in a subject in need thereof, such methods including the step of administering to the subject a composition that includes at least one component selected from among a peptide of the present invention, a polynucleotide encoding such a peptide, exosomes or APCs presenting such peptides, and CTLs that can recognize cells presenting such peptides on their surface.

[0018]

The applicability of the present disclosure extends to any of a number of diseases relating to or arising from TOPK overexpression, such as cancers expressing TOPK, examples of which include, but are not limited to, AML, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, colorectal cancer, diffuse-type gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal carcinoma, SCLC and soft tissue tumor.

Objects and features of the invention will become more fully apparent when the following detailed description is read in conjunction with the accompanying figures and examples. It is to be understood that both the foregoing summary of the present invention and the following detailed description are of exemplified embodiments, and not restrictive of the present invention or other alternate embodiments of the present invention.

[0019]

In particular, while the invention is described herein with reference to a number of specific embodiments, it will be appreciated that the description is illustrative of the invention and is not constructed as limiting of the invention. Various modifications and applications may occur to those who are skilled in the art, without departing from the spirit and the scope of the invention, as described by the appended claims. Likewise, other objects, features, benefits and advantages of the present invention will be apparent from this summary and certain embodiments described below, and will be readily apparent to those skilled in the art. Such objects, features, benefits and advantages will be apparent from the above in conjunction with the accompanying examples, data, figures and all reasonable inferences to be drawn therefrom, alone or with consideration of the references incorporated herein.

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 [1] to [8],
(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 [1] to [8], and
(c) introducing into a CD8-positive T cell a polynucleotide/polynucleotides encoding T cell receptor (TCR) subunit polypeptides, wherein the TCR formed by said TCR subunit polypeptides is capable of binding to a complex of an HLA antigen and the peptide of any one of [1] to [8] on a cell surface.
[15] An isolated APC that presents on its surface a complex of an HLA antigen and the peptide of any one of [1] to [8].
[16] The APC of [15], which is induced by the method of [13].
[17] An isolated CTL that targets the peptide of any one of [1] to [8].
[18] The CTL of [17], which is induced by the method of [14].
[19] A method of inducing an immune response against cancer in a subject, said method comprising the step of administering to the subject a composition comprising the peptide of any one of [1] to [8], an immunologically active fragment thereof, or a polynucleotide encoding the peptide or the fragment.
[20] An antibody or immunologically active fragment thereof against the peptide of any one of [1] to [8].
[21] A vector comprising a nucleotide sequence encoding the peptide of any one of [1] to [8].
[22] A host cell transformed or transfected with the vector of [21].
[23] A diagnostic kit comprising a peptide of any one of [1] to [8], the polynucleotide of [9] or the antibody of [20].
[24] A method of screening for a peptide having an ability to induce a CTL that has specific cytotoxic activity against a cell that presents a fragment derived from TOPK, wherein the method comprises the steps of:
(i) providing a candidate sequence consisting of an amino acid sequence modified by substituting, deleting, inserting and/or adding one, two or several amino acid residues to an original amino acid sequence, wherein the original amino acid sequence is selected from the group consisting of SEQ ID NOs: 2, 3, 6, 27, 28, 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76;
(ii) selecting a candidate sequence that does not have substantial significant homology with the peptides derived from any known human gene products other than TOPK;
(iii) contacting a peptide consisting of the candidate sequence selected in step (ii) with an antigen presenting cell;
(iv) contacting the antigen presenting cell of step (iii) with a CD8-positive T cell; and

[0067] The present invention also contemplates the addition of 1, 2 or several amino acids can also be added to the N and/or C-terminus of the present peptides. Such modified peptides having CTL inducibility are also included in the present invention.
[0068] For example, the present invention 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 selected from among SEQ ID NOs: 2 to 24 and 42 to 60,
(ii) an amino acid sequence in which 1, 2 or several amino acid(s) are modified in the amino acid sequence selected from the group consisting of SEQ ID NOs: 2 to 24 and 42 to 60, wherein the peptide has an ability to induce a cytotoxic T lymphocyte,
(iii) the amino acid sequence of (ii), wherein, in the context of HLA-A24, 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 NOs is or is modified to be an amino acid selected from the group consisting of phenylalanine, tyrosine, methionine, and tryptophan, and
(b) the C-terminal amino acid of said SEQ ID NOs is or is modified to be an amino acid selected from the group consisting of phenylalanine, leucine, isoleucine, tryptophan, and methionine, and
(iv) the amino acid sequence of (ii), wherein, in the context of HLA-A2, the amino acid sequence has one or both of the following characteristics:
(c) the second amino acid from the N-terminus of said SEQ ID NO is or is modified to be an amino acid selected from the group consisting of leucine and methionine; and
(d) the C-terminal amino acid of said SEQ ID NO is or is modified to be an amino acid selected from the group consisting of valine and leucine.
[0069] Moreover, the present invention 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 selected form among SEQ ID NOs: 25 to 40 and 61 to 84,
(ii') an amino acid sequence in which 1, 2 or several amino acid(s) are modified in the amino acid sequence selected from the group consisting of SEQ ID NOs: 25 to 40 and 61 to 84, wherein the peptide has an ability to induce a cytotoxic T lymphocyte,
(iii') the amino acid sequence of (ii'), wherein, in the context of HLA-A24, 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 NOs is or is modified to be an amino acid selected from the group consisting of phenylalanine, tyrosine, methionine, and tryptophan, and
(b') the C-terminal amino acid of said SEQ ID NOs is or is modified to be an amino

acid selected from the group consisting of phenylalanine, leucine, isoleucine, tryptophan, and methionine.
[0070] (iv') the amino acid sequence of (ii'), wherein, in the context of HLA-A2, the amino acid sequence has one or both of the following characteristics:
(c') the second amino acid from the N-terminus of said SEQ ID NOs is or is modified to be an amino acid selected from the group consisting of leucine and methionine; and
(d') the C-terminal amino acid of said SEQ ID NOs is or is modified to be an amino acid selected from the group consisting of valine and leucine.
[0071] These peptides bind with HLA antigens on APCs to be presented on APCs as complex with an HLA antigen when those peptides are contacted APCs. Alternatively, those peptides are introduced into APCs and processed to fragments having an amino acid sequence selected from among (i)-(iv) and (i')-(iv') in APCs to be presented on APCs as complexes with HLA antigens, when those peptides are contacted with APCs. Consequently, CTLs specific to such peptides are induced.
[0072] However, when the peptide sequence is identical to a portion of the amino acid sequence of an endogenous or exogenous protein having a different function, negative side effects such as autoimmune disorders and/or allergic symptoms against specific substances may be induced. Therefore, it may be desirable to first perform homology searches using available databases to avoid situations in which the sequence of the peptide matches the amino acid sequence of another protein. When it becomes clear from the homology searches that no peptide identical to or having 1 or 2 amino acid differences as compared to the objective peptide exists in nature, the objective peptide can be modified in order to increase its binding affinity with HLA antigens, and/or increase its CTL inducibility without any danger of such side effects.
[0073] Although peptides having high binding affinity to the HLA antigens as described above are expected to be highly effective, the candidate peptides, which are selected according to the presence of high binding affinity as an indicator, are further examined for the presence of CTL inducibility. Herein, the phrase "CTL inducibility" indicates the ability of the peptide to induce cytotoxic T lymphocytes (CTLs) when presented on antigen-presenting cells (APCs). Further, "CTL inducibility" includes the ability of the peptide to induce CTL activation, CTL proliferation, promote lysis of target cells by CTL, and to increase IFN-gamma production by CTL.
[0074] Confirmation of CTL inducibility is accomplished by inducing APCs carrying human MHC antigens (for example, B-lymphocytes, macrophages, and dendritic cells (DCs)), or more specifically DCs derived from human peripheral blood mononuclear leukocytes, and after stimulation of APCs with a test peptides, mixing APCs with CD8 positive T cells to induce CTLs, and then measuring the IFN-gamma produced and released by CTL against the target cells. As the reaction system, transgenic animals

(iv) contacting the antigen presenting cell of step (iii) with a CD8 positive T cell; and
(v) identifying the peptide of which CTL inducibility is same to or higher than a peptide consisting of the original amino acid sequence.
Herein, the activity to be assayed may include MHC binding activity, APC or CTL inducibility and cytotoxic activity. Preferably, the activity of the peptide to be assayed is CTL inducibility.
[0087] III. Preparation of TOPK Peptides:
The peptides of the present invention can be prepared using well known techniques. For example, the peptides can be prepared synthetically, using recombinant DNA technology or chemical synthesis. The peptides of the present invention can be synthesized individually or as longer polypeptides including two or more peptides. The peptides can then be isolated i.e., purified or isolated so as to be substantially free of other naturally occurring host cell proteins and fragments thereof, or any other chemical substances.
[0088] The peptides of the present invention may contain modifications, such as glycosylation, side chain oxidation, or phosphorylation, provided the modifications do not destroy the biological activity of the original peptide. Other illustrative modifications include incorporation of one or more D-amino acids or other amino acid mimetics that can be used, for example, to increase the serum half life of the peptides.
[0089] Peptides of the present invention can be obtained through chemical synthesis based on the selected amino acid sequence. Examples of conventional peptide synthesis methods that can be adapted for the synthesis include:
(i) Peptide Synthesis, Interscience, New York, 1966;
(ii) The Proteins, Vol. 2, Academic Press, New York, 1976;
(iii) Peptide Synthesis (in Japanese), Maruzen Co., 1975;
(iv) Basics and Experiment of Peptide Synthesis (in Japanese), Maruzen Co., 1985;
(v) Development of Pharmaceuticals (second volume) (in Japanese), Vol. 14 (peptide synthesis), Hirokawa, 1991;
(vi) WO99/67288; and
(vii) Barany G. & Merrifield R.B., Peptides Vol. 2, "Solid Phase Peptide Synthesis", Academic Press, New York, 1980, 100-118.
[0090] Alternatively, the present peptides can be obtained adapting any known genetic engineering method for producing peptides (e.g., Morrison J, J Bacteriology 1977, 132: 349-51; Clark-Curtiss & Curtiss, Methods in Enzymology (eds. Wu et al.) 1983, 101: 347-62). For example, first, a suitable vector harboring a polynucleotide encoding the objective peptide in an expressible form (e.g., downstream of a regulatory sequence corresponding to a promoter sequence) is prepared and transformed into a suitable host cell. The host cell is then cultured to produce the peptide of interest. The peptide can

that contains:
(a) a peptide of the present invention;
(b) a polynucleotide encoding the peptide of the present invention in an expressible form;
(c) an APC presenting a peptide of the present invention on its surface;
(d) an exosome presenting a peptide of the present invention on its surface; or
(e) a cytotoxic T cell of the present invention.
[0168] In the context of the present invention, a cancer over-expressing TOPK can be treated with these active ingredients. Examples of such cancer include, but are not limited to, AML, bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, colorectal cancer, diffuse-type gastric cancer, NSCLC, lymphoma, osteosarcoma, prostate cancer, renal carcinoma, SCLC and soft tissue tumor. Accordingly, prior to the administration of the vaccines or pharmaceutical compositions or agents including the aforementioned active ingredients, it is preferable to confirm whether the expression level of TOPK in the subject to be treated is enhanced. Thus, in one embodiment, the present invention provides a method for treating cancer (over)expressing TOPK in a patient in need thereof, such method including the steps of:
i) determining the expression level of TOPK in biological sample(s) obtained from a subject with the cancer to be treated;
ii) comparing the expression level of TOPK with normal control; and
iii) administrating at least one component selected from among (a) to (e) described above to a subject with cancer over-expressing TOPK as compared with normal control.
[0169] Alternatively, the present invention provides a vaccine or pharmaceutical composition including at least one component selected from among (a) to (e) described above, to be administered to a subject having cancer over-expressing TOPK. In other words, the present invention further provides a method for identifying a subject to be treated with the TOPK polypeptide of the present invention, such method including the step of determining an expression level of TOPK in subject-derived biological sample(s), wherein an increase of the level compared to a normal control level of the gene indicates that the subject may have cancer which may be treated with the TOPK polypeptide of the present invention. The methods of treating cancer of the present invention will be described in more detail in below.
[0170] Any subject-derived cell or tissue can be used for the determination of TOPK expression so long as it includes the objective transcription or translation product of TOPK. Examples of suitable samples include, but are not limited to, bodily tissues and fluids, such as blood, sputum and urine. Preferably, the subject-derived cell or tissue

Claims

1. An isolated peptide of less than 15 amino acids selected from the group consisting of (a) and (b) below:
(a) an isolated peptide having cytotoxic T lymphocyte (CTL) inducibility comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76, and
(b) an isolated peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76, in which 1 or 2 amino acid(s) are substituted, inserted, and/or added, wherein the peptide has 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 an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76 is substituted to be an amino acid selected from the group consisting of leucine and methionine; and
(b) the C-terminal amino acid of an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76 is substituted to be an amino acid selected from the group consisting of valine and leucine.

3. The isolated peptide of claim 1 or 2, wherein said peptide is a nonapeptide or a decapeptide.

4. An isolated peptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76.

5. An isolated polynucleotide encoding the isolated peptide of any one of claims 1 to 4.

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

7. A pharmaceutical composition comprising:
(a) one or more peptide(s) of any one of claims 1 to 4;
(b) one or more polynucleotide(s) of claim 5;
(c) one or more APC(s) that present a complex of the peptide of any one of claims 1 to 4 and an HLA antigen on their surface;
(d) one or more exosome(s) that present a complex of the peptide of any one of claims 1 to 4 and an HLA antigen on their surface; or
(e) one or more CTL(s) that can recognize a cell presenting a complex of the peptide of any one of claims 1 to 4 and an HLA antigen on their surface,
in combination with a pharmaceutically acceptable carrier, wherein the

pharmaceutical composition is formulated for the treatment and/or prophylaxis of cancer, the prevention of a postoperative recurrence thereof, and/or the induction of an immune response against cancer.

8. The pharmaceutical composition of claim 7, wherein said pharmaceutical composition is formulated for administration to a subject whose HLA antigen is HLA-A2.

9. An *in vitro* method for inducing an antigen-presenting cell (APC) with CTL inducibility, said method comprising the step selected from the group consisting of:
(a) contacting an APC with the peptide of any one of claims 1 to 4 *in vitro*, and
(b) introducing a polynucleotide encoding the peptide of any one of claims 1 to 4 into an APC.

10. An *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 4,
(b) co-culturing a CD8-positive T cells with an exosome that presents on its surface a complex of an HLA antigen and the peptide of any one of claims 1 to 4, and
(c) introducing into a CD8-positive T cell a polynucleotide/polynucleotides encoding a T cell receptor (TCR) subunit polypeptides, wherein the TCR formed by said TCR subunit polypeptides is capable of binding to a complex of an HLA antigen and the peptide of any one of claims 1 to 4 on a cell surface.

11. An isolated APC that presents on its surface a complex of an HLA antigen and the peptide of any one of claims 1 to 4.

12. The APC of claim 11, which is induced by the method of claim 9.

13. An isolated CTL that targets the peptide of any one of claims 1 to 4.

14. The CTL of claim 13, which is induced by the method of claim 10.

15. A composition for use in inducing an immune response against cancer in a subject in need thereof, wherein the composition comprises the peptide of any one of claims 1 to 4 or a polynucleotide encoding the peptide.

16. Use of a composition comprising the peptide of any one of claims 1 to 4 or a polynucleotide encoding the peptide in the manufacture of a medicament for treating cancer by inducing an immune response against cancer in a subject in need thereof.

17. A vector comprising a nucleotide sequence encoding the peptide of any one of claims 1 to 4.

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 4 or the polynucleotide of claim 5.

20. A method of screening for a peptide having an ability to induce a CTL that has specific cytotoxic activity against a cell that presents a fragment derived from TOPK, wherein the method comprises the steps of:
(i) providing a candidate sequence consisting of an amino acid sequence modified by substituting, inserting and/or adding one or two amino acid residues to an original amino acid sequence, wherein the original amino acid sequence is selected from the group consisting of SEQ ID NOs: 42, 45, 47, 50, 51, 53, 54, 62, 63, 64, 66, 71, 72 and 76;
(ii) selecting a candidate sequence that does not have substantial significant homology with the peptides derived from any known human gene products other than TOPK;
(iii) contacting a peptide consisting of the candidate sequence selected in step (ii) with an antigen presenting cell;
(iv) contacting the antigen presenting cell of step (iii) with a CD8-positive T cell; and
(v) identifying the peptide of which CTL inducibility is same to or higher than a peptide consisting of the original amino acid sequence.