cancer, 10 out of 11 cholangiocellular carcinoma, 7 out of 19 esophageal cancer, 21 out of 22 NSCLC, all of 6 ovarian cancer, 17 out of 36 prostate cancer, 6 out of 11 renal carcinoma and all of 15 SCLC .
KNTC2 expression is validly elevated in 30 out of 32 bladder cancer, 47 out of 56 breast cancer, all of 10 cervical cancer, 16 out of 22 cholangioncellular carcinoma, 17 out of 37 CML, 3 out of 10 colorectal cancer, 11 out of 46 esophagus cancer, 15 out of 19 NSCLC, 7 out of 8 lymphoma, 20 out of 24 osteosarcoma, 3 out of 5 ovarian cancer, all of 2 pancreatic cancer, 15 out of 37 prostate cancer, 14 out of 19 renal carcinoma, all of 15 SCLC and 40 out of 59 soft tissue tumor.
TTK expression is validly elevated in all of 27 bladder cancer, 25 out of 30 breast cancer, 15 out of 16 cervical cancer, all of 10 cholangiocellular carcinoma, 5 out of 7 CML, 6 out of 10 colorectal cancer, 24 out of 44 esophageal cancer, 8 out of 15 liver cancer, all of 12 NSCLC, all of 6 lymphoma, 13 out of 16 osteoblastoma, 12 out of 17 prostate cancer, all of 15 SCLC and 16 out of 33 soft tissue tumor.
URLC10 expression is validly elevated in all of 29 bladder cancer, 15 out of 16 cervical cancer, all of 7 cholangiocellular carcinoma, 7 out of 19 esophageal cancer, all of 3 gastric cancer, 24 out of 27 NSCLC, 15 out of 19 osteosarcoma, 4 out of 5 pancreatic cancer, 33 out of 43 soft tissue tumor .

[0011] The present disclosure is based, at least in part, on the identification of specific epitope peptides of the gene products of these genes (CDH3, EPHA4, ECT2, HIG2, INHBB, KIF20A, KNTC2, TTK and URLC10) which possess the ability to induce cytotoxic T lymphocytes (CTLs) specific to the corresponding molecules. As discussed in detail below, Peripheral Blood Mononuclear Cells (PBMC) of healthy donor were stimulated using HLA-A*2402 or HLA-A*0201 binding candidate peptides derived from CDH3, EPHA4, ECT2, HIG2, INHBB, KIF20A, KNTC2, TTK or URLC10. CTL clones and/or lines were then established with specific cytotoxicity against the HLA-A24 or HLA-A2 positive target cells pulsed with each of the candidate peptides. These results demonstrate that these peptides are HLA-A24 or HLA-A2 restricted epitope peptides that can induce potent and specific immune responses against cells expressing CDH3, EPHA4, ECT2, HIG2, INHBB, KIF20A, KNTC2, TTK or URLC10.

[0011a] In a first aspect, there is provided an isolated peptide consisting of peptides comprising the amino acid sequences of SEQ ID NO: 271.

[0011b] In a second aspect, there is provided a peptide having cytotoxic T cell inducibility, wherein said peptide consists of the amino acid sequence SEQ ID NO: 271, in which 1 or 2 amino acids are substituted.

[0011c] In a third aspect, there is provided an exosome that presents on its surface a complex comprising a peptide and an HLA-A2, wherein the peptide is selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted.

[0011d] In a fourth aspect, there is provided an antigen-presenting cell, which comprises a complex formed between an HLA-A2 and a peptide selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted.

[0012] Accordingly, the present disclosure provides methods for treating or preventing a disease associated with the over-expression of CDH3, EPHA4, ECT2, HIG2, INHBB, KIF20A, KNTC2, TTK or URLC10, e.g. cancer. Such methods involve the step of administering to a subject in need thereof a CDH3, EPHA4, ECT2, HIG2, INHBB, KIF20A, KNTC2, TTK and/or URLC10 polypeptides of the disclosure. Administration of such peptide(s) results in the induction of anti-tumor immunity is induced by the administration of these polypeptides. Thus, the present disclosure provides methods for inducing anti-tumor immunity in a subject, such methods involving the step of admin-

istering to the subject the CDH3, EPHA4, ECT2, HIG2, INHBB, KIF20A, KNTC2, TTK and/or URLC10 polypeptides, as well as pharmaceutical compositions for treating or preventing a disease associated with the over-expression of CDH3, EPHA4, ECT2, HIG2, INHBB, KIF20A, KNTC2, TTK and/or URLC10, e.g. cancer, that include the CDH3, EPHA4, ECT2, HIG2, INHBB, KIF20A, KNTC2, TTK and URLC10 polypeptides. Examples of such cancers include, but are not limited to., bladder cancer, breast cancer, cervical cancer, cholangincellular carcinoma, CML, colorectal cancer, endometriosis, esophageal cancer, gastric cancer, diffused type gastric cancer, liver cancer, NSCLC, lymphoma, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal carcinoma, SCLC, soft tissue tumor and testicular tumor.

[0012a] In a fifth aspect, there is provided a pharmaceutical composition for use in treating or preventing cancer, said composition comprising one or more peptides of the first aspect or a polynucleotide encoding the peptides.

[0012b] In a sixth aspect, there is provided an *in vitro* method of inducing an antigen-presenting cell having a high cytotoxic T cell inducibility, said method comprising the step of (a) or (b) below:

(a) contacting an HLA-A2 positive antigen-presenting cell with a peptide; or

(b) transferring a gene comprising a polynucleotide encoding a peptide to an HLA-A2 positive antigen-presenting cell, wherein the peptide is selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted.

[0012c] Provided is an an *in vitro* method of inducing a cytotoxic T cell by contacting a T cell with any one of the peptides of the first aspect.

[0012d] In a seventh aspect, there is provided an *in vitro* method of inducing a cytotoxic T cell, comprising the steps of (a) and (b) below:

(a) contacting an HLA-A2 positive antigen-presenting cell with a peptide, wherein the peptide is selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted; and

(b) mixing the antigen-presenting cell of step (a) with a $CD8^+$ T cell and co-culturing.

[0012e] In an eighth aspect, there is provided an isolated cytotoxic T cell, which is induced by the method of the seventh aspect, or which is transduced with the nucleic acids encoding the TCR subunits polypeptides binding with a peptide in the context of HLA-A2, wherein the peptide is selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted.

[0012f] In a ninth aspect, there is provided an antigen-presenting cell, which is induced by the method of the sixth aspect.

[0012g] In a tenth aspect, there is provided a vaccine for use in inhibiting proliferation of cancer, wherein the vaccine comprises any one of the peptides of the first aspect as the active ingredient.

[0012h] In an eleventh aspect, there is provided use of at least one ingredient selected from the group consisting of (a) to (e) below:

(a) one or more types of peptides selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted;

(b) one or more types of polynucleotides encoding any one of the peptide(s) of (a) in an expressible form;

(c) an APC that presents on its cell surface a complex of any one of the peptides of (a) and an HLA-A2;

(d) an exosome that presents on its cell surface a complex of any one of the peptides of (a) and an HLA-A2; and

(e) a CTL that targets any one of the peptides of (a)

in the manufacture of a medicament for treating or preventing a cancer expressing HLA-A2.

[0012i] In a twelfth aspect, there is provided use of the peptide selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted

in the manufacture of a vaccine for inhibiting cancer expressing HLA-A2.

[0013]

The present disclosure further provides methods for preventing post-surgery recurrence of the disease mentioned above.

Regarding the specific aims and objectives recited above, it will be understood by those skilled in the art that one or more aspects of this

disclosure can meet certain objectives, while one or more other aspects can meet certain other objectives. Each objective may not apply equally, in all its respects, to every aspect of this disclosure. As such, the objects herein can be viewed in the alternative with respect to any one aspect of this disclosure.

[0014]

Additional objects and features of the disclosure will become more fully apparent when the following detailed description is read in conjunction with the accompanying figures and examples. However, it is to be understood that both the foregoing summary of the disclosure and the following detailed description are of preferred embodiments, and not restrictive of the disclosure or other alternate embodiments of the disclosure. In particular, while the disclosure is described herein with reference to a number of specific embodiments, it will be appreciated that the description is illustrative of the disclosure and is not constructed as limiting of the disclosure. Various modifications and applications may occur to those who are skilled in the art, without departing from the spirit and the scope of the disclosure, as described by the appended claims. Likewise, other objects, features, benefits and advantages of the present disclosure 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.

Brief Description of Drawings

[0015]

Various aspects and applications of the present invention will become apparent to the skilled artisan upon consideration of the brief description of the figures and the

CLAIMS

[Claim 1] An isolated peptide consisting of the amino acid sequences of SEQ ID NO: 271.

[Claim 2] A peptide having cytotoxic T cell inducibility, wherein said peptide consists of the amino acid sequence of SEQ ID NO: 271, in which 1 or 2 amino acids are substituted.

[Claim 3] The peptide of claim 2, wherein the second amino acid from the N-terminus is leucine or methionine.

[Claim 4] The peptide of claim 2 or 3, wherein the C-terminal amino acid is valine or leucine.

[Claim 5] A pharmaceutical composition for use in treating or preventing cancer, said composition comprising one or more peptides of any one of claims 1 to 4 or a polynucleotide encoding the peptides.

[Claim 6] A pharmaceutical composition for use of claim 5, wherein the cancer is selected from the group consisting of bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, CML, colorectal cancer, endometriosis, esophageal cancer, gastric cancer, diffused type gastric cancer, liver, NSCLC, lymphoma, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal carcinoma, SCLC, soft tissue tumor and testicular tumor.

[Claim 7] An exosome that presents on its surface a complex comprising a peptide and an HLA-A2, wherein the peptide is selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted.

[Claim 8] The exosome of claim 7, wherein the HLA-A2 is HLA-A0201.

[Claim 9] An in vitro method of inducing an antigen-presenting cell having a high cytotoxic T cell inducibility, said method comprising the step of (a) or (b) below:

(a) contacting an HLA-A2 positive antigen-presenting cell with a peptide; or

(b) transferring a gene comprising a polynucleotide encoding a peptide to an HLA-A2 positive antigen-presenting cell, wherein the peptide is selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted.

[Claim 10] An in vitro method of inducing a cytotoxic T cell, comprising the steps of (a) and (b) below:

(a) contacting an HLA-A2 positive antigen-presenting cell with a peptide, wherein the peptide is selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted; and

(b) mixing the antigen-presenting cell of step (a) with a CD8+ T cell and co-culturing.

[Claim 11] An isolated cytotoxic T cell, which is induced by the method of claim 10, or which is transduced with the nucleic acids encoding the TCR subunits polypeptides binding with a peptide in the context of HLA-A2, wherein the peptide is selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid

sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted.

[Claim 12] An antigen-presenting cell, which comprises a complex formed between an HLA-A2 and a peptide selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted.

[Claim 13] An antigen-presenting cell, which is induced by the method of claim 9.

[Claim 14] A vaccine for use in inhibiting proliferation of cancer, wherein the vaccine comprises the peptide of any one of claims 1 to 4 as the active ingredient.

[Claim 15] The vaccine of claim 14, wherein the cancer is selected from the group consisting of bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, CML, colorectal cancer, endometriosis, esophageal cancer, gastric cancer, diffused type gastric cancer, liver, NSCLC, lymphoma, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal carcinoma, SCLC, soft tissue tumor and testicular tumor.

[Claim 16] The vaccine of claim 15, which is formulated for administration to a subject whose HLA antigen is HLA-A2.

[Claim 17] The vaccine of claim 16, wherein the HLA-A2 is HLA-A0201.

[Claim 18] Use of at least one ingredient selected from the group consisting of (a) to (e) below:

(a) one or more types of peptides selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted;

(b) one or more types of polynucleotides encoding the peptide(s) of any one of (a) in an expressible form;

(c) an APC that presents on its cell surface a complex of the peptide of any one of (a) and an HLA-A2;

(d) an exosome that presents on its cell surface a complex of the peptide of any one of (a) and an HLA-A2; and

(e) a CTL that targets the peptide of any one of (a)

in the manufacture of a medicament for treating or preventing a cancer expressing HLA-A2.

[Claim 19] The use of claim 18, wherein the cancer is selected from the group consisting of bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, CML, colorectal cancer, endometriosis, esophageal cancer, gastric cancer, diffused type gastric cancer, liver, NSCLC, lymphoma, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal carcinoma, SCLC, soft tissue tumor and testicular tumor.

[Claim 20] Use of the peptide selected from the group consisting of following (i) and (ii):

(i) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272; and

(ii) a peptide of less than 15 amino acids comprising an amino acid sequence of SEQ ID NO: 288, 271 or 272 in which 1 or 2 amino acids are substituted

in the manufacture of a vaccine for inhibiting cancer expressing HLA-A2.

[Claim 21] The use of claim 20, wherein the cancer is selected from the group consisting of bladder cancer, breast cancer, cervical cancer, cholangiocellular carcinoma, CML, colorectal cancer, endometriosis, esophageal cancer, gastric cancer, diffused type gastric cancer, liver, NSCLC, lymphoma, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, renal carcinoma, SCLC, soft tissue tumor and testicular tumor.