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Disclosure ~~of the Invention~~

[Problems to be Solved by the Disclosure~~Invention~~]

An objective to be achieved by the present disclosure~~invention~~ is to develop means for implementing immunotherapy that suppresses cancer growth by enhancing the immunity of cancer patients against cancer, as a therapeutic method for metastatic or intractable cancers which are difficult to be treated by surgical therapy, chemotherapy, and radiotherapy for treating lung cancer, biliary tract cancer, *etc.* The present inventors identified peptides that are derived from proteins specifically and highly expressed in cancer, and which are presented to killer T cells by HLA-A2, thereby enabling immunotherapy to be applicable to about 30% of Japanese patients with various cancers that highly express CDCA1.

[Means for Solving the Problems]

The present inventors identified the CDCA1 gene (GenBank Accession No. NM_145697), which is highly expressed in lung cancer, from cDNA microarray analysis of lung cancer tissues. CDCA1 expression in normal tissues is observed only in the testis isolated from the immune system. In order to examine whether or not anti-tumor immunity is induced by CDCA1 specific killer T cells, HLA-A2 transgenic mice expressing HLA-A2 which is possessed by approximately 30% of the Japanese were used. Specifically, herein, the inventors examined whether or not HLA-A2 restricted peptide-specific killer T cells are induced when HLA-A2 transgenic mice are immunized with mouse bone marrow-derived dendritic cells pulsed with human CDCA1 peptides having an HLA-A2 binding motif. Whether CDCA1 peptide-specific killer T cells are induced in the spleen cells of immunized mice or not was examined using ELISPOT assay to detect γ-interferon (IFN-γ) produced by killer T cells activated from recognizing peptides presented by HLA-A2. As a result, two types of novel CDCA1 peptides that can be applied to immunotherapy targeting HLA-A2 positive cancer patients were identified. Furthermore, it was confirmed that cancer patient-derived and healthy donor-derived CTLs

activated by these peptides show cytolytic activity against CDCA1 expressing cells. That is, the peptides are expected to be recognized by HLA-A2 restricted human killer T cells and applicable to cancer immunotherapy for HLA-A2 positive cancer patients.

In one aspect, there is provided an isolated peptide of less than 15 amino acids selected from the group consisting of:

(A) a peptide comprising the amino acid sequence of SEO ID NO: 2;

(B) a peptide which comprises the amino acid sequence of SEO ID NO: 2, in which one or two amino acid(s) are substituted, deleted, inserted, and/or added, and wherein the peptide shows cytotoxic (killer) T cell-inducing activity; and

(C) a peptide consisting of the amino acid sequence of SEO ID NO: 2.

In one aspect, there is provided a vaccine for use in inducing immunity against cancer expressing CDCA1, which comprises one or more peptide(s) as defined herein as an active ingredient.

In one aspect, there is provided a vaccine for use in treating and/or preventing cancer expressing CDCA1, which comprises one or more peptide(s) as defined herein as an active ingredient.

In one aspect, there is provided a vaccine for use in inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, wherein said vaccine comprises one or more peptide(s) as defined herein as an active ingredient.

In one aspect, there is provided a vaccine for use in inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, wherein said vaccine comprises one or more polynucleotide(s) encoding the peptides as defined herein as an active ingredient.

In one aspect, there is provided a vaccine for use in inducing a cytotoxic (killer) T cell, wherein said vaccine comprises one or more peptide(s) as defined herein as an active ingredient.

In one aspect, there is provided an antibody against the peptide as defined herein.

In one aspect, there is provided a helper T cell, a cytotoxic (killer) T cell, or an immunocyte population comprising them, which is induced using the peptide as defined herein.

In one aspect, there is provided an antigen-presenting cell that presents a complex comprising the peptide as defined herein and an HLA antigen.

In one aspect, there is provided an exosome that presents a complex comprising the peptide as defined herein and an HLA antigen.

In one aspect, there is provided an in vitro method for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, which comprises the step of contacting an antigen-presenting cell with the peptide as defined herein.

In one aspect, there is provided an in vitro method for inducing an antigen-presenting cell

that shows cytotoxic (killer) T cell-inducing activity, which comprises the step of introducing a polynucleotide encoding the peptide as defined herein into an antigen presenting cell.

In one aspect, there is provided an in vitro method for inducing a cytotoxic (killer) T cell, which comprises the step of co-culturing an antigen-presenting cell contacted with the peptide as defined herein and a CD8+ T cell.

In one aspect, there is provided the use of the peptide as defined herein for the manufacture of an agent for inducing immunity against cancer expressing CDCA1.

In one aspect, there is provided the use of the peptide as defined herein for the manufacture of an agent for treating and/or preventing cancer expressing CDCA1.

In one aspect, there is provided the peptide as defined herein for use in induction of immunity against cancer expressing CDCA1.

In one aspect, there is provided the peptide as defined herein for use in treatment and/or prevention of cancer expressing CDCA1.

More specifically, the present disclosure~~invention~~ provides the following:

[1] a peptide of (A) or (B) below:

(A) a peptide including the amino acid sequence of SEQ ID NO: 1 or 2;

(B) a peptide which includes the amino acid sequence of SEQ ID NO: 1 or 2, wherein one, two, or several amino acid(s) are substituted, deleted, inserted, and/or added, and wherein the peptide shows cytotoxic (killer) T cell-inducing activity;

[2] the peptide of [1], wherein the second amino acid from the N terminus is leucine or methionine;

[3] the peptide of [1], wherein the C-terminal amino acid is valine or leucine;

[4] an agent for inducing immunity against cancer, which includes one or more peptide(s) of [1] as an active ingredient;

[5] an agent for treating and/or preventing cancer, which includes one or more peptide(s) of [1] as an active ingredient;

[6] an agent for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, wherein said agent includes one or more peptide(s) of [1] as an active ingredient;

[7] an agent for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, wherein said agent includes one or more polynucleotide(s) encoding the peptides of [1] as an active ingredient;

[8] an agent for inducing a cytotoxic (killer) T cell, wherein said agent includes one or more peptide(s) of [1] as an active ingredient;

[9] an antibody against the peptide of [1];

[10] a helper T cell, a cytotoxic (killer) T cell, or an immunocyte population including them, which is induced using the peptide of [1];

[11] an antigen-presenting cell that presents a complex including the peptide of [1] and an HLA antigen;

[12] the antigen-presenting cell of [11], which is induced by the agent of [6] or [7];

[13] an exosome that presents a complex including the peptide of [1] and an HLA antigen;

[14] the exosome of [13], wherein the HLA antigen is HLA-A2 (HLA-A2*0201);

[15] a method for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, which includes the step of contacting an antigen-presenting cell with the peptide of [1];

[16] a method for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, which includes the step of introducing a polynucleotide encoding the

CLAIMS

1. A peptide of (A) or (B) below:
(A) a peptide comprising the amino acid sequence of SEQ ID NO: 1 or 2;
(B) a peptide which comprises the amino acid sequence of SEQ ID NO: 1 or 2, wherein one, two, or several amino acid(s) are substituted, deleted, inserted, and/or added, and wherein the peptide shows cytotoxic (killer) T cell-inducing activity.

2. The peptide of claim 1, wherein the second amino acid from the N terminus is leucine or methionine.

3. The peptide of claim 1, wherein the C-terminal amino acid is valine or leucine.

4. An agent for inducing immunity against cancer, which comprises one or more peptide(s) of claim 1 as an active ingredient.

5. An agent for treating and/or preventing cancer, which comprises one or more peptide(s) of claim 1 as an active ingredient.

6. An agent for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, wherein said agent comprises one or more peptide(s) of claim 1 as an active ingredient.

7. An agent for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, wherein said agent comprises one or more polynucleotide(s) encoding the peptides of claim 1 as an active ingredient.

8. An agent for inducing a cytotoxic (killer) T cell, wherein said agent comprises one or more peptide(s) of claim 1 as an active ingredient.

9. An antibody against the peptide of claim 1.

10. A helper T cell, a cytotoxic (killer) T cell, or an immunocyte population comprising them, which is induced using the peptide of claim 1.

11. An antigen-presenting cell that presents a complex comprising the peptide of claim 1 and an HLA antigen.

12. The antigen-presenting cell of claim 11, which is induced by the agent of claim 6 or 7.

13. An exosome that presents a complex comprising the peptide of claim 1 and an HLA antigen.

14. The exosome of claim 13, wherein the HLA antigen is HLA-A2 (HLA-A2*0201).

15. A method for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, which comprises the step of contacting an antigen-presenting cell with the peptide of claim 1.

16. A method for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, which comprises the step of introducing a polynucleotide encoding the peptide of claim 1 into an antigen presenting cell.

17. A method for inducing a cytotoxic (killer) T cell, which comprises the step of contacting a T cell with the peptide of claim 1.

18. A method for inducing immunity against cancer, which comprises the step of administering the peptide of claim 1 to a subject.

19. A method for treating and/or preventing cancer, which comprises the step of administering the peptide of claim 1 to a subject.

20. Use of the peptide of claim 1 for the production of an agent for inducing immunity against cancer.

21. Use of the peptide of claim 1 for the production of an agent for treating and/or preventing cancer.

22. The peptide of claim 1, for induction of immunity against cancer.

23. The peptide of claim 1, for treatment and/or prevention of cancer.

Claims

1. An isolated peptide of less than 15 amino acids selected from the group consisting of:
(A) a peptide comprising the amino acid sequence of SEO ID NO: 2;
(B) a peptide which comprises the amino acid sequence of SEO ID NO: 2, in which one or two amino acid(s) are substituted, deleted, inserted, and/or added, and wherein the peptide shows cytotoxic (killer) T cell-inducing activity; and
(C) a peptide consisting of the amino acid sequence of SEO ID NO: 2.

2. The peptide of claim 1, wherein the peptide is selected from the group consisting of:
(A) a peptide consisting of the amino acid sequence of SEO ID NO: 2; and
(B) a peptide which consists of the amino acid sequence of SEO ID NO: 2, in which one or two amino acid(s) are substituted, deleted, inserted, and/or added, and wherein the peptide shows cytotoxic (killer) T cell-inducing activity.

3. The peptide of claim 1 or 2, wherein the second amino acid from the N terminus is leucine or methionine.

4. The peptide of any one of claims 1 to 3, wherein the C-terminal amino acid is valine or leucine.

5. A vaccine for use in inducing immunity against cancer expressing CDCA1, which comprises one or more peptide(s) of any one of claims 1 to 4 as an active ingredient.

6. A vaccine for use in treating and/or preventing cancer expressing CDCA1, which comprises one or more peptide(s) of any one of claims 1 to 4 as an active ingredient.

7. A vaccine for use in inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, wherein said vaccine comprises one or more peptide(s) of any one of claims 1 to 4 as an active ingredient.

8. A vaccine for use in inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, wherein said vaccine comprises one or more polynucleotide(s) encoding the peptides of any one of claims 1 to 4 as an active ingredient.

9. A vaccine for use in inducing a cytotoxic (killer) T cell, wherein said vaccine comprises one or more peptide(s) of any one of claims 1 to 4 as an active ingredient.

10. An antibody against the peptide of any one of claims 1 to 4.

11. A helper T cell, a cytotoxic (killer) T cell, or an immunocyte population comprising them, which is induced using the peptide of any one of claims 1 to 4.

12. An antigen-presenting cell that presents a complex comprising the peptide of any one of claims 1 to 4 and an HLA antigen.

13. The antigen-presenting cell of claim 12, which is induced by the vaccine of claim 7 or 8.

14. An exosome that presents a complex comprising the peptide of any one of claims 1 to 4 and an HLA antigen.

15. The exosome of claim 14, wherein the HLA antigen is HLA-A2 (HLA-A*0201).

16. An in vitro method for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, which comprises the step of contacting an antigen-presenting cell with the peptide of any one of claims 1 to 4.

17. An in vitro method for inducing an antigen-presenting cell that shows cytotoxic (killer) T cell-inducing activity, which comprises the step of introducing a polynucleotide encoding the peptide of any one of claims 1 to 4 into an antigen presenting cell.

18. An in vitro method for inducing a cytotoxic (killer) T cell, which comprises the step of co-culturing an antigen-presenting cell contacted with the peptide of any one of claims 1 to 4 and a CD8+ T cell.

19. Use of the peptide of any one of claims 1 to 4 for the manufacture of an agent for inducing immunity against cancer expressing CDCA1.

20. Use of the peptide of any one of claims 1 to 4 for the manufacture of an agent for treating and/or preventing cancer expressing CDCA1.

21. The peptide of any one of claims 1 to 4 for use in induction of immunity against cancer expressing CDCA1.

22. The peptide of any one of claims 1 to 4 for use in treatment and/or prevention of cancer expressing CDCA1.

23. The vaccine of claim 5 or 6, or the use of claim 19 or 20, or the peptide of claim 21 or 22, wherein said cancer expressing CDCA1 is selected from the group consisting of lung cancer, cholangiocellular carcinoma, bladder cancer, renal cell carcinoma, prostate cancer, chronic myelogenous leukemia, malignant lymphoma, cervical cancer, osteosarcoma, breast cancer, soft tissue sarcoma, and colon cancer.