was hardly expressed in adult normal organs. Further, CDH3 was observed to be also highly expressed in most cases of cholangiocellular carcinoma, gastric cancer, colon cancer, non-small cell lung cancer, testicular cancer, cervical cancer, osteosarcoma, soft tissue sarcoma, and the like. This fact suggests that CDH3 can be a cancer-specific antigen in many cancers.

HLA-A2 is frequently observed in human populations regardless of the race, and about 30% of the Japanese carry HLA-A2. Therefore, if a peptide presented to killer T cells by HLA-A2 can be identified, it can be widely applied to not only Japanese but also western Caucasians and the like. Accordingly, the identification of cancer antigen peptides presented to killer T cells by HLA-A2 is an important task. It may be highly beneficial to apply such cancer antigen peptides to immunotherapy for lung cancer, whose morbidity and mortality rates are high all over the world.

Prior art document information relevant to the invention of the present application is shown below.

[Non-patent Document 1] Nakamura, T., *et al.*, Oncogene 23: 2385-2400 (2004)
[Non-patent Document 2] Obama, K., *et al.*, Hepatology 41: 1339-1348 (2005)
[Non-patent Document 3] Taniuchi, K., *et al.*, Cancer Res 65: 3092-3099 (2005)
[Non-patent Document 4] Soler, A. P., *et al.*, Cancer 86: 1263-1272 (1999)
[Non-patent Document 5] Paredes, J., *et al.*, Clin Cancer Res 11: 5869-5877 (2005)
[Non-patent Document 6] Ingunn, M., *et al.*, J Clin Oncol 22: 1242-1252 (2004)
[Non-patent Document 7] Glenn, L., *et al.*, J Cell Biol 139: 1025-1032 (1997)
[Non-patent Document 8] Bauer, R., *et al.*, Exp. Mol. Pathol. 81: 224-230 (2006)
[Non-patent Document 9] Muzon-Guerra, M.F., *et al.* Cancer 103: 960-969 (2005)
[Non-patent Document 10] Marck, V.V., *et al.*, Cancer Res. 65: 8774-8783 (2005)

Disclosure ~~of the Invention~~

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

An objective to be achieved by the present ~~invention~~disclosure is to develop means to realize an immunotherapy that suppresses cancer growth by improving the immunity of cancer patients against cancer, as a novel therapy for metastatic or intractable cancers which are difficult to be treated by surgical treatments, chemotherapy, and radiotherapy, which are used to treat pancreatic cancer, cholangiocellular carcinoma, gastric cancer, colon cancer, non-small cell lung cancer, and the like. The present ~~invention~~disclosure provides identified peptides that are derived from proteins specifically and highly expressed in cancers and are presented to killer T cells by HLA-A2. This enables an immunotherapy that can be applied to about 30% of Japanese patients with various cancers that highly express CDH3.

[Means for Solving the Problems]

The present inventors identified CDH3 (GenBank Accession No. NM_001793) as a gene highly expressed in pancreatic cancer, by cDNA microarray analysis of pancreatic cancer tissues. In order to examine whether or not antitumor immunity is induced by CDH3 specific killer T cells, HLA-A2 transgenic mice expressing HLA-A2, which is carried by about 30% of the Japanese, were used. Specifically, HLA-A2 transgenic mice were immunized with mouse bone marrow-derived dendritic cells pulsed with a human CDH3 peptide having an HLA-A2 binding motif to examine whether HLA-A2 restricted peptide-specific killer T cells would be induced. The ELISPOT method was used to detect γ-interferon (IFN-γ) produced by killer T cells that had been activated by recognizing the peptide presented by HLA-A2, and thereby examine whether killer T cells specific to the CDH3 peptide were induced or not in spleen cells of the immunized mice. As a result, the present inventors identified two novel CDH3 peptides applicable to immunotherapy for HLA-A2 positive cancer patients. In addition, it was revealed that CDH3 responsive CTLs induced by using these peptides had cytotoxicity specific to cancer cells expressing endogenous CDH3 and HLA-A2 molecules, and that the CTLs recognized the target cells in an HLA-class I-restricted manner. Moreover, it was also revealed that the growth of tumors transplanted to NOD/SCID mice was significantly suppressed by intravenously injecting CD8 positive cells induced by the peptides (CTL adoptive immunity method).

In one aspect, there is provided an isolated peptide of the following (A) or (B):

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

(B) a peptide consisting of an amino acid sequence of SEQ ID NO:1 or 2, in which one or two amino acid(s) are substituted and wherein the peptide has an activity to induce a cytotoxic (killer) T cell.

In one aspect, there is provided an agent for inducing immunity against cancer, comprising one or more peptide(s) as defined above as an active ingredient.

In one aspect, there is provided an agent for treating and/or preventing cancer, comprising one or more peptide(s) as defined above as an active ingredient.

In one aspect, there is provided an agent for inducing an antigen presenting cell having cytotoxic (killer) T cell- inducing activity, said agent comprising:

(A) one or more peptide(s) as defined above; or

(B) one or more polynucleotide(s) encoding the peptide as defined above,

as an active ingredient.

In one aspect, there is provided an agent for inducing a cytotoxic (killer) T cell, comprising one or more peptide(s) as defined above as an active ingredient.

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

In one aspect, there is provided an isolated cytotoxic (killer) T cell, or an isolated group of immunocytes comprising the cytotoxic (killer) T cells, which is induced by using the peptide as defined above.

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

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

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

In one aspect, there is provided the use of the peptide as defined above for manufacture of a medicament for treating and/or preventing cancer.

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

(1) a peptide of the following (A) or (B):

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

(B) a peptide including an 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 has an activity to induce a cytotoxic (killer) T cell;

(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, including one or more peptide(s) of (1) as an active ingredient;

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

(6) an agent for inducing an antigen presenting cell having cytotoxic (killer) T cell-inducing activity, including one or more peptide(s) of (1) as an active ingredient;

(7) an agent for inducing an antigen presenting cell having cytotoxic (killer) T cell-inducing activity, including one or more polynucleotide(s) encoding the peptide of (1) as an active ingredient;

CLAIMS

1. A peptide of the following (A) or (B):
(A) a peptide comprising an amino acid sequence of SEQ ID NO: 1 or 2;
(B) a peptide comprising an 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 has an activity to induce a cytotoxic (killer) T cell.

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, comprising one or more peptide(s) of claim 1 as an active ingredient.

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

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

7. An agent for inducing an antigen presenting cell having cytotoxic (killer) T cell-inducing activity, comprising one or more polynucleotide(s) encoding the peptide of claim 1 as an active ingredient.

8. An agent for inducing a cytotoxic (killer) T cell, comprising 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 a group of immunocytes comprising these cells, which is induced by 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-A*0201).

15. A method for inducing an antigen presenting cell having cytotoxic (killer) T cell-inducing activity, comprising a step of contacting the antigen presenting cell with the peptide of claim 1.

16. A method for inducing an antigen presenting cell having cytotoxic (killer) T cell-inducing activity, comprising a step of transfecting a polynucleotide encoding the peptide of claim 1 into an antigen presenting cell.

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

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

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

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

21. Use of the peptide of claim 1 for manufacture of a medicament for treating and/or preventing cancer.

CLAIMS

1. An isolated peptide of the following (A) or (B):

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

(B) a peptide consisting of an amino acid sequence of SEQ ID NO:1 or 2, in which one or two amino acid(s) are substituted and wherein the peptide has an activity to induce a cytotoxic (killer) T cell.

2. The peptide of Claim 1, wherein the second amino acid from the N-terminus of the amino acid sequence of the SEQ ID NO: I or 2 is replaced with leucine or methionine.

3. The peptide of Claim 1 or 2, wherein the C-terminal amino acid of the amino acid sequence of the SEQ ID NO: 1 or 2 is replaced with valine or leucine.

4. An agent for inducing immunity against cancer, comprising one or more peptide(s) of any one of Claims 1 to 3 as an active ingredient.

5. An agent for treating and/or preventing cancer, comprising one or more peptide(s) of any one of Claims 1 to 3 as an active ingredient.

6. An agent for inducing an antigen presenting cell having cytotoxic (killer) T cell-inducing activity, said agent comprising:

(A) one or more peptide(s) of any one of Claims 1 to 3; or

(B) one or more polynucleotide(s) encoding the peptide of any one of Claims 1 to 3,

as an active ingredient.

7. An agent for inducing a cytotoxic (killer) T cell, comprising one or more peptide(s) of any one of Claims 1 to 3 as an active ingredient.

8. An isolated antibody against the peptide of any one of Claims 1 to 3.

9. An isolated cytotoxic (killer) T cell, or an isolated group of immunocytes comprising the cytotoxic (killer) T cells, which is induced by using the peptide of any one of Claims 1 to 3.

10. An isolated antigen presenting cell that presents a complex comprising the peptide of any one of Claims 1 to 3 and an HLA antigen.

11. The antigen presenting cell of Claim 10, which is induced by the agent of Claim 6.

12. An isolated exosome that presents a complex comprising the peptide of any one of Claims 1 to 3 and an HLA antigen.

13. The exosome of Claim 12, wherein the HLA antigen is HLA-A2(HLA-A*0201).

14. Use of the peptide of any one of Claims 1 to 3 for manufacture of an agent for inducing immunity against cancer.

15. Use of the peptide of any one of Claims 1 to 3 for manufacture of a medicament for treating and/or preventing cancer.