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Disclosure ~~of the Invention~~

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

An objective of the present ~~invention~~disclosure is to develop a means for carrying out

immunotherapy that suppresses cancer growth by enhancing the anti-cancer immunity of cancer patients as a novel therapeutic method for metastatic or intractable cancers that are difficult to be treated by surgical therapy, chemotherapy, and radiotherapy which are conducted as therapeutic methods for biliary tract cancer, lung cancer, pancreatic cancer, and such. More specifically, an objective of the present ~~invention~~disclosure is to identify peptides that are derived from proteins highly and specifically expressed in cancers and can induce strong immunoreaction against the above-mentioned cancers without causing adverse events in cancer patients, and to apply these peptides in tumor immunotherapy. The present ~~invention~~disclosure enables immunotherapy for approximately 30% of the Japanese patients with the above-mentioned cancers, by identifying peptides that are derived from a protein highly and specifically expressed in the above-mentioned cancers and are presented to killer T cells by HLA-A2.

[Means for Solving the Problems]

Herein, the present inventors induced FOXM1 peptide-specific killer T cells by *in vitro* stimulation of human CD8 positive killer T cells by co-culturing them with human peripheral blood monocyte-derived dendritic cells pulsed with human FOXM1 peptides which have an HLA-A2 binding motif. Whether or not there was induction of killer T cells specific to each FOXM1 peptide was examined by detecting γ-interferon (IFN-γ) produced by the killer T cells activated from recognition of the peptide presented by HLA-A2 using ELISPOT assay. As a result, novel FOXM1 peptides that are potentially candidate target antigens applicable to immunotherapy were identified. Furthermore, it was revealed that FOXM1-responsive CTLs induced using the aforementioned peptides have specific cytotoxicity against cancer cells expressing endogenous FOXM1 and HLA-A2 molecules, and that the CTLs recognize target cells in an HLA class I-restricted manner.

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

(A) a peptide of less than 15 amino acids, said peptide comprising the amino acid sequence of any one of SEQ ID NOs: 1 to 3;

(B) a peptide of less than 15 amino acids, said peptide comprising the amino acid sequence of any one of SEQ ID NOs: 1 to 3 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.

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

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

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

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

In one aspect, there is provided an agent for use in inducing a cytotoxic (killer) T cell, wherein said agent comprises 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, an isolated helper T cell, or an isolated immunocyte population comprising them, which is induced 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 in the production of an agent for inducing immunity against cancer.

In one aspect, there is provided the use of the peptide as defined above in the production of an agent for treating and/or preventing cancer.

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

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

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

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

(A) a peptide including the amino acid sequence of any one of SEQ ID NOs: 1 to 3;

(B) a peptide which includes the amino acid sequence of any one of SEQ ID NOs: 1 to 3, 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]

CLAIMS

1. A peptide of (A) or (B) below:
(A) a peptide comprising the amino acid sequence of any one of SEQ ID NOs: 1 to 3;
(B) a peptide which comprises the amino acid sequence of any one of SEQ ID NOs: 1 to 3, 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 peptide 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 cytotoxic (killer) T cell, a helper 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-A*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 in the production of an agent for inducing immunity against cancer.

21. Use of the peptide of claim 1 in 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 (A) or (B) below:

(A) a peptide of less than 15 amino acids, said peptide comprising the amino acid sequence of any one of SEQ ID NOs: 1 to 3;

(B) a peptide of less than 15 amino acids, said peptide comprising the amino acid sequence of any one of SEQ ID NOs: 1 to 3 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.

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 any one of SEQ ID NOs: 1 to 3; and

(B) a peptide consisting of the amino acid sequence of any one of SEQ ID NOs: 1 to 3 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. An agent for use in inducing immunity against cancer, which comprises one or more peptide(s) of any one of Claims 1 to 4 as an active ingredient.

6. An agent for use in treating and/or preventing cancer, which comprises one or more peptide(s) of any one of Claims 1 to 4 as an active ingredient.

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

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

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

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

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

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

13. The isolated antigen-presenting cell of Claim 12, which is induced by the agent of Claim 7 or 8.

14. An isolated 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. Use of the peptide of any one of Claims 1 to 4 in the production of an agent for inducing immunity against cancer.

17. Use of the peptide of any one of Claims 1 to 4 in the production of an agent for treating and/or preventing cancer.

18. The peptide of any one of Claims 1 to 4, for use in induction of immunity against cancer.

19. The peptide of any one of Claims 1 to 4, for use in treatment and/or prevention of cancer.