[Non Patent Literature 6] Shimizu K. et al., "Cancer Research", (USA), 2016; 76 (13): 3756-3766

[Summary]

[Technical Problem]

[0007]

An object of the present disclosure is to provide aAVC stably expressing NY-ESO-1 or a fragment thereof.

[Solution to Problem]

[0008]

The present inventors have conducted considerable diligent studies on the preparation of aAVC expressing NY-ESO-1 as a cancer antigen, and as a result, successfully obtained aAVC stably expressing NY-ESO-1. Specifically, the present inventors have found a problem of constitutively expressed NY-ESO-1, which is reduction in expression level and positive rate with increase in the number of culture days, and solved the problem by diligent studies. Specifically, the present inventors have found that cells inducibly expressing NY-ESO-1 with an inducible promoter (particularly, a drug inducible promoter) show a higher expression level of NY-ESO-1 than in the case of constitutively expressing NY-ESO-1, and successfully obtained aAVC with stably and highly expressing NY-ESO-1 under the control of an inducible promoter (Example 2-2). Specifically, the present disclosure provides aAVC that can be used for treating a

cancer, a method for producing the aAVC, a pharmaceutical composition comprising the aAVC, a method for treating a cancer with the aAVC, etc.

[0009]

Specifically, the present disclosure may include the following aspects as a medically or industrially useful substance or method.

[0010]

[1] A human-derived cell, comprising a polynucleotide encoding CD1d and a polynucleotide encoding NY-ESO-1 or a fragment thereof, wherein the polynucleotide encoding NY-ESO-1 or a fragment thereof is operably linked to an inducible promoter.

[2] The cell according to [1], wherein the NY-ESO-1 is human NY-ESO-1.

[3] The cell according to [1] or [2], wherein the CD1d is human CD1d.

[4] The cell according to any one of [1] to [3], wherein the inducible promoter is a drug inducible promoter.

[5] The cell according to [4], wherein the drug inducible promoter is a tetracycline inducible promoter.

[6] The cell according to [5], wherein the tetracycline inducible promoter is TRE3G promoter.

[7] The cell according to any one of [1] to [6], wherein the human-derived cell is a normal cell.

[24] The method according to [23], wherein the immune checkpoint inhibitor is a PD-1 immune checkpoint inhibitor or a CTLA-4 immune checkpoint inhibitor.

[25] A method for producing a pharmaceutical composition for use in treating a cancer, comprising the steps of:

thawing a frozen product comprising a cloned human-derived cell comprising a polynucleotide encoding CD1d and a polynucleotide encoding NY-ESO-1 or a fragment thereof, wherein the polynucleotide encoding NY-ESO-1 or a fragment thereof is operably linked to an inducible promoter;

propagating the human cell contained in the frozen product to induce the expression of the NY-ESO-1 or the fragment thereof; and

loading α-GalCer on the surface of the cell.

[0011]

The aAVC-NY-ESO-1 cell of the present disclosure and the pharmaceutical composition of the present disclosure can be used in treating a cancer.

[0011a] In one aspect, the present disclosure provides a human-derived cell, comprising a polynucleotide encoding CD1d and a polynucleotide encoding NY-ESO-1 or a fragment thereof, wherein the polynucleotide encoding NY-ESO-1 or a fragment thereof is operably linked to an inducible promoter. In another aspect, the present disclosure provides a pharmaceutical composition comprising a cell

according to the disclosure. In another aspect, the present disclosure provides a use of a cell according to the disclosure in the manufacture of a pharmaceutical composition for treating a cancer. In another aspect, the present disclosure provides an *in vitro* method for producing a cell for treating a cancer, comprising the step of culturing a cell according to the disclosure in the presence of an inducer of an inducible promoter, thereby inducing the expression of NY-ESO-1 or a fragment thereof. In another aspect, the present disclosure provides an *in vitro* method for producing a cell for treating a cancer, comprising the step of: introducing a polynucleotide encoding CD1d and a polynucleotide encoding NY-ESO-1 or a fragment thereof to a human-derived cell, wherein the polynucleotide encoding NY-ESO-1 or a fragment thereof is operably linked to an inducible promoter; or introducing a polynucleotide encoding NY-ESO-1 or a fragment thereof to a human-derived cell endogenously expressing CD1d, wherein the polynucleotide encoding NY-ESO-1 or a fragment thereof is operably linked to an inducible promoter. In another aspect, the present disclosure provides a use of a cell according to the disclosure in the manufacture of a pharmaceutical composition for use in combinatorial therapy for treating a cancer, wherein said pharmaceutical composition is to be administered in combination with an immune checkpoint inhibitor to a

subject. In another aspect, the present disclosure provides a use of a cell according to the disclosure in the manufacture of a first pharmaceutical composition and use of an immune checkpoint inhibitor in the manufacture of a second pharmaceutical composition, wherein the first and second pharmaceutical compositions are to be used in combination therapy to treat a cancer in a subject. In another aspect, the present disclosure provides a use of a cell according to the disclosure and an immune checkpoint inhibitor in the manufacture of a pharmaceutical composition for combination therapy for treating a cancer.

[BRIEF DESCRIPTION OF THE DRAWINGS]

[0012]

[Figure 1-1] Figure 1-1 shows the antigen-specific T cell inducing effect of aAVC(3T3)-NY-ESO-1 cells in terms of the number of NY-ESO-1-specific T cells in mice given the aAVC(3T3)-NY-ESO-1 cells. The ordinate depicts the number of spots in 4×10^5 spleen cells counted with

What is claimed is:

1. A human-derived cell, comprising a polynucleotide encoding CD1d and a polynucleotide encoding NY-ESO-1 or a fragment thereof, wherein the polynucleotide encoding NY-ESO-1 or a fragment thereof is operably linked to an inducible promoter.

2. The cell according to claim 1, wherein the NY-ESO-1 is human NY-ESO-1.

3. The cell according to claim 1 or 2, wherein the CD1d is human CD1d.

4. The cell according to any one of claims 1 to 3, wherein the inducible promoter is a drug inducible promoter.

5. The cell according to claim 4, wherein the drug inducible promoter is a tetracycline inducible promoter.

6. The cell according to claim 5, wherein the tetracycline inducible promoter is TRE3G promoter.

7. The cell according to any one of claims 1 to 6, wherein the human-derived cell is a normal cell.

8. The cell according to claim 7, wherein the human-derived cell is a cell derived from a human embryonic kidney cell 293 (HEK293) cell.

9. The cell according to any one of claims 1 to 8, expressing CD1d and NY-ESO-1 or a fragment thereof.

10. The cell according to claim 9, wherein an expression level of the NY-ESO-1 or the fragment thereof is 245 ng to 45000 ng per 10^6 cells.

11. The cell according to claim 9 or 10, wherein a CD1d ligand is loaded on the surface of the cell.

12. The cell according to claim 11, wherein the CD1d ligand is α-GalCer.

13. A pharmaceutical composition comprising a cell according to claim 11 or 12.

14. The pharmaceutical composition according to claim 13 for use in therapy.

15. Use of a cell according to claim 11 or 12 in the manufacture of a pharmaceutical composition for treating a cancer.

16. The cell according to claim 11 or 12 for use in therapy.

17. An *in vitro* method for producing a cell for treating a cancer, comprising the step of culturing a cell according to any one of claims 1 to 8 in the presence of an inducer of an inducible promoter, thereby inducing the expression of NY-ESO-1 or a fragment thereof.

18. The method according to claim 17, further comprising the step of loading α-GalCer onto the surface of the cell.

19. An *in vitro* method for producing a cell for treating a cancer, comprising the step of:

introducing a polynucleotide encoding CD1d and a polynucleotide encoding NY-ESO-1 or a fragment thereof to a human-derived cell, wherein the polynucleotide encoding NY-ESO-1 or a fragment thereof is operably linked to an inducible promoter; or

introducing a polynucleotide encoding NY-ESO-1 or a fragment thereof to a human-derived cell endogenously expressing CD1d, wherein the polynucleotide encoding NY-ESO-1 or a fragment thereof is operably linked to an inducible promoter.

20. The method according to claim 19, further comprising the step of culturing the cell obtained in the step in the presence of an inducer of the inducible promoter, thereby inducing the expression of NY-ESO-1 or a fragment thereof.

21. The method according to claim 20, further comprising the step of loading α-GalCer onto the surface of the cell.

22. Use of a cell according to claim 11 or 12 in the manufacture of a pharmaceutical composition for use in combinatorial therapy for treating a cancer, wherein said pharmaceutical composition is to be administered in combination with an immune checkpoint inhibitor to a subject.

23. Use of a cell according to claim 11 or 12 in the manufacture of a first pharmaceutical composition and use of an immune checkpoint inhibitor in the manufacture of a second pharmaceutical composition, wherein the first and second pharmaceutical compositions are to be used in combination therapy for treating a cancer in a subject.

24. Use of a cell according to claim 11 or 12 and an immune checkpoint inhibitor in the manufacture of a

pharmaceutical composition for combination therapy for treating a cancer.

25. The use according to claim 22, wherein the immune checkpoint inhibitor is a PD-1 immune checkpoint inhibitor or a CTLA-4 immune checkpoint inhibitor.