tumor can be temporarily treated. Furthermore, preventive measures against recurrence have not been discussed. Accordingly, an object of the present ~~invention~~disclosure is to provide an enhancer for endogenous T-cells or B-cells having a memory function, a malignant tumor recurrence inhibitor, and an inducer for inducing a memory function in endogenous T-cells or B-cells in order to continue to reject malignant tumor over a long period of time.

Means to Solve the Object

[0008a]

In one aspect, the present disclosure provides the use of a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7) and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19) in the manufacture of a medicament for inhibiting malignant tumor recurrence or malignant tumor metastasis, wherein the nucleic acid delivery vehicle is an immune cell, and the immune cell has a cell surface molecule that recognizes a malignant tumor antigen, and wherein the malignant tumor recurrence or malignant tumor metastasis is a malignant tumor recurrence or malignant tumor metastasis ascribable to a malignant tumor cell having resistance to an ability to accumulate to malignant tumor cells.

[0008b]

In another aspect, the present disclosure provides an enhancer for T-cells or B-cells having a memory function in an administration subject, comprising a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7), and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19), wherein the nucleic acid delivery vehicle is an immune cell or a virus.

[0008c]

In another aspect, the present disclosure provides a pharmaceutical composition for enhancing T-cells or B-cells having a memory function in an administration subject comprising the enhancer for T-cells or B-cells having a memory function in an administration subject as disclosed herein and a pharmaceutically acceptable additive.

[0008d]

In another aspect, the present disclosure provides the use of the enhancer as disclosed herein in the manufacture of a medicament for enhancing T-cells or B-cells having a memory function in an administration subject.

[0008e]

In another aspect, the present disclosure provides an inducer for inducing a memory function in endogenous T-cells or B-cells in an administration subject, comprising a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7), and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19), wherein the nucleic acid delivery vehicle is an immune cell or a virus.

[0008f]

In another aspect, the present disclosure provides a pharmaceutical composition for inducing a memory function in endogenous T-cells or B-cells in an administration subject comprising the inducer for inducing a memory function in endogenous T-cells or B-cells in an administration subject as disclosed herein and a pharmaceutically acceptable additive.

[0008g]

In another aspect, the present disclosure provides the enhancer as disclosed herein for use in therapy.

[0008h]

In another aspect, the present disclosure provides the enhancer as disclosed herein for use in therapy.

[0008i]

In another aspect, the present disclosure provides the inducer as disclosed herein for use in therapy.

[0008j]

In another aspect, the present disclosure provides the use of the inducer as disclosed herein in the manufacture of a medicament for inducing a memory function in endogenous T-cells or B-cells in an administration subject.

[0008k]

In another aspect, the present disclosure provides the use of a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7), and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19) in the manufacture of a medicament for inhibiting a malignant tumor formation, wherein the nucleic acid delivery vehicle is an immune cell, and the immune cell has a cell surface molecule that recognizes a malignant tumor antigen, and wherein the malignant tumor is a malignant tumor ascribable to a malignant tumor cell having resistance to an ability of the cell surface molecule to accumulate to malignant tumor cells.

[0009]

The present inventors have studied the further possibilities of the previously developed T-cells expressing CAR, IL-7 and CCL19 and consequently found that: the administration of the T-cells to a subject induces a memory function not only in the administered T-cells but in endogenous T-cells in the subject (host) and increases the absolute number of cells having a memory function; and in a recurrence model experiment of

malignant tumor, this administration suppresses malignant tumor formation in cells having no antigen that is recognized by CAR. The present inventors have further found that use of TCR instead of CAR or use of a virus instead of T-cells also produces similar effects. On the basis of these findings, the present invention has been completed.

[0010]

Specifically, the present invention is as follows.

(1) An enhancer for T-cells or B-cells having a memory function in an administration subject, comprising a nucleic acid delivery vehicle, a nucleic acid encoding

CLAIMS

1. Use of a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7) and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19) in the manufacture of a medicament for inhibiting malignant tumor recurrence or malignant tumor metastasis, wherein the nucleic acid delivery vehicle is an immune cell, and the immune cell has a cell surface molecule that recognizes a malignant tumor antigen, and wherein the malignant tumor recurrence or malignant tumor metastasis is a malignant tumor recurrence or malignant tumor metastasis ascribable to a malignant tumor cell having resistance to an ability to accumulate to malignant tumor cells.

2. The use according to claim 1, wherein the immune cell has a cytotoxicity against malignant tumor cells.

3. The use according to claim 1 or 2, wherein the malignant tumor recurrence or malignant tumor metastasis is a malignant tumor recurrence or malignant tumor metastasis ascribable to a malignant tumor cell having no malignant tumor antigen that is specifically recognized by the cell surface molecule.

4. The use according to any one of claims 1 to 3, wherein the cell surface molecule that recognizes a malignant tumor antigen is a chimeric antigen receptor (CAR).

5. The use according to any one of claims 1 to 3, wherein the cell surface molecule that recognizes a malignant tumor antigen is a T-cell receptor (TCR).

6. The use according to any one of claims 1 to 5, wherein the immune cell is a T-cell.

7. Use of a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7) and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19) in the manufacture of a medicament for inhibiting malignant tumor recurrence or malignant tumor metastasis, wherein the nucleic acid delivery vehicle is a virus.

8. The use according to any one of claims 1 to 7, wherein the malignant tumor recurrence or malignant tumor metastasis inhibitor is to be intratumorally or intravenously administered in an administration subject.

~~1~~9. An enhancer for T-cells or B-cells having a memory function in an administration subject, comprising a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7), and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19)~~.~~

~~2. The enhancer for T-cells or B-cells having a memory function in an administration subject according to claim 1~~, wherein the nucleic acid delivery vehicle is ~~at least one member selected from~~ an immune cell~~,~~ or a virus~~, an anaerobe,~~

~~a liposome, a mesenchymal stem cell (MSC), and a nanoparticle~~.

~~3~~10. The enhancer for T-cells or B-cells having a memory function in an administration subject according to claim ~~1 or 2~~9, wherein the ~~nucleic acid delivery vehicle~~ immune cell or the virus has an ability to accumulate to malignant tumor cells, or an ability to proliferate specifically in malignant tumor cells.

~~4~~11. The enhancer for T-cells or B-cells having a memory function in an administration subject according to ~~any one of~~ claim~~s 1~~ 9 or~~to 3~~10, wherein the ~~nucleic acid delivery vehicle~~ immune cell or the virus has a cytotoxicity against malignant tumor cells.

~~5~~12. The enhancer for T-cells or B-cells having a memory function in an administration subject according to ~~any one of~~ claim~~s 1~~ 9~~to 4~~, wherein the nucleic acid delivery vehicle is an immune cell, and the immune cell has a cell surface molecule that recognizes a malignant tumor antigen.

~~6~~13. The enhancer for T-cells or B-cells having a memory function in an administration subject according to claim ~~5~~12, wherein the cell surface molecule that recognizes a malignant tumor antigen is a chimeric antigen receptor (CAR) ~~or a T cell receptor (TCR)~~.

14. The enhancer for T-cells or B-cells having a memory function in an administration subject according to claim 12,

wherein the cell surface molecule that recognizes a malignant tumor antigen is a T-cell receptor (TCR).

~~7~~15. The enhancer for T-cells or B-cells having a memory function in an administration subject according to any one of claims 12 to 14~~5 or 6~~, wherein the immune cell is a T-cell.

~~8~~16. The enhancer for T-cells or B-cells having a memory function in an administration subject according to any one of claims ~~1 to 7~~9 to 15, wherein the T-cells or B-cells having a memory function are central memory T-cells.

~~9~~17. A pharmaceutical composition for enhancing T-cells or B-cells having a memory function in an administration subject comprising the ~~an~~ enhancer for T-cells or B-cells having a memory function in an administration subject according to any one of claims ~~1~~ 9 to ~~8~~ 16 and a pharmaceutically acceptable additive.

18. The enhancer according to any one of claims 9 to 16 for use in therapy.

19. Use of the enhancer according to any one of claims 9 to 16 in the manufacture of a medicament for enhancing T-cells or B-cells having a memory function in an administration subject.

20. The use of claim 19, wherein the enhancer is to be intratumorally or intravenously administered in an administration subject.

21. An inducer for inducing a memory function in endogenous T-cells or B-cells in an administration subject, comprising a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7), and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19), wherein the nucleic acid delivery vehicle is an immune cell or a virus.

22. A pharmaceutical composition for inducing a memory function in endogenous T-cells or B-cells in an administration subject comprising the inducer for inducing a memory function in endogenous T-cells or B-cells in an administration subject according to claim 21 and a pharmaceutically acceptable additive.

23. The inducer according to claim 21, for use in therapy.

24. Use of the inducer according to claim 21 in the manufacture of a medicament for inducing a memory function in endogenous T-cells or B-cells in an administration subject.

~~10~~25. ~~A malignant tumor recurrence inhibitor comprising~~ Use of a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7), and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19) in the manufacture of a medicament for inhibiting a malignant tumor formation~~.~~

~~11. The malignant tumor recurrence inhibitor according to claim 10, wherein the nucleic acid delivery vehicle is at least one member selected from an immune cell, a virus, an anaerobe, a liposome, a mesenchymal stem cell (MSC), and a nanoparticle.~~

~~12. The malignant tumor recurrence inhibitor according to claim 10 or 11, wherein the nucleic acid delivery vehicle has an ability to accumulate to malignant tumor cells, or an ability to proliferate specifically in malignant tumor cells.~~

~~13. The malignant tumor recurrence inhibitor according to any one of claims 10 to 12, wherein the nucleic acid delivery vehicle has a cytotoxicity against malignant tumor cells.~~

~~14. The malignant tumor recurrence inhibitor according to any one of claims 10 to 13~~, wherein the nucleic acid delivery vehicle is an immune cell, and the immune cell has a cell surface molecule that recognizes a malignant tumor antigen, and wherein the malignant tumor is a malignant tumor ascribable to a malignant tumor cell having resistance to an ability of the cell surface molecule to accumulate to malignant tumor cells.

~~15~~26. The ~~malignant tumor recurrence inhibitor~~use according to claim ~~14~~25, wherein ~~the nucleic acid delivery vehicle is an immune cell having a cell surface molecule that recognizes a malignant tumor cell antigen, and~~ the malignant

tumor ~~recurrence~~ is a malignant tumor ~~recurrence~~ ascribable to a malignant tumor cell having no malignant tumor antigen that is specifically recognized by the cell surface molecule.

~~16. The malignant tumor recurrence inhibitor according to claim 14 or 15, wherein the cell surface molecule that recognizes a malignant tumor cell antigen is a chimeric antigen receptor (CAR) or a T-cell receptor (TCR).~~

~~17. The malignant tumor recurrence inhibitor according to any one of claims 14 to 16, wherein the immune cell is a T-cell.~~

~~18. The malignant tumor recurrence inhibitor according to claim 11, wherein the nucleic acid delivery vehicle is an oncolytic virus.~~

~~19. A pharmaceutical composition comprising a malignant tumor recurrence inhibitor according to any one of claims 10 to 18 and a pharmaceutically acceptable additive.~~

~~20. An inducer for inducing a memory function in T-cells or B-cells in an administration subject, comprising a nucleic acid delivery vehicle, a nucleic acid encoding interleukin-7 (IL-7), and a nucleic acid encoding chemokine (C-C motif) ligand 19 (CCL19).~~