modified vaccinia viruses with attenuated toxicity such as modified vaccinia Ankara (MVA), LC16m8 (derived from the Lister strain), and New York vaccinia virus (NYVAC, derived from the Copenhagen vaccinia strain) were developed. Vaccines that are applicable to various diseases have been developed based on these vaccinia viruses. In particular, vaccinia virus strains such as Western Reserve (WR), NYVAC, Wyeth, and Lister are also being developed as oncolytic viruses.

Disclosure of Invention

Aspects of the invention are defined in the independent claims. Some optional features of the invention are defined in the dependent claims.

Thus, it may be possible to provide a recombinant vaccinia virus comprising a cancer therapeutic gene and optionally having suppressed expression of some genes therein, and a pharmaceutical composition for treating cancer, comprising same as an active ingredient.

It may be particularly possible to provide a recombinant vaccinia virus, comprising a gene encoding soluble programmed cell death protein-1 (sPD-1) and a gene encoding hyaluronidase.

In addition, it may be possible to provide a pharmaceutical composition for treating cancer, comprising the recombinant vaccinia virus as an active ingredient.

In addition, it may be possible to provide a method for treating cancer, comprising a step of administering, to an individual, a composition that contains the recombinant vaccinia virus as an active ingredient.

colorectal tumor model, IHD-W-VV05 and IHD-W-VV06, and then measuring tumor growth.

Fig. 31 illustrates results obtained by intratumorally administering, to a mouse melanoma model, IHD-W-VV05 and IHD-W-VV06, and then measuring tumor growth.

Fig. 32 illustrates results obtained by intratumorally administering, to a mouse lung tumor model, IHD-W-VV05 and IHD-W-VV06, and then measuring tumor growth.

Fig. 33 illustrates results obtained by intratumorally administering, to a mouse melanoma model, IHD-W-VV01 and IHD-W-VV06, and then measuring tumor growth.

Fig. 34 illustrates results obtained by intratumorally administering, to a mouse lung tumor model, IHD-W-VV01 and IHD-W-VV06, and then measuring tumor growth.

Fig. 35 illustrates results obtained by intratumorally administering, to a mouse lung tumor model, WR-VV01 and WR-VV06, and then measuring tumor growth.

Fig. 36 illustrates results obtained by intratumorally administering, to a mouse lung tumor model, Lister-VV01 and Lister-VV06, and then measuring tumor growth.

Fig. 37 illustrates results obtained by determining *in vitro* cell-killing ability of IHD-W-VV06, WR-VV06, and Lister-VV06.

Best Mode for Carrying out the Invention

In an aspect, there is provided a recombinant vaccinia virus comprising a gene encoding soluble programmed cell death protein-1 (sPD-1) and a gene encoding hyaluronidase. The recombinant vaccinia virus may further comprise a gene encoding IL-12.

The term "sPD-1" as used herein refers to an extracellular domain or a fragment

The recombinant vaccinia virus is a vaccinia virus comprising the sPD-1 gene and the hyaluronidase gene. The vaccinia virus may comprise the IL-12 gene. Here, the sPD-1 gene, the hyaluronidase gene, and/or the IL-12 gene may be inserted into the vaccinia virus' genome. In addition, the genes may also be inserted at different positions of the vaccinia virus' genome; however, such genes may be inserted at the same or similar positions. As an example, each of such genes may be inserted at the TK, K3L, or VGF position of the vaccinia virus. Preferably, the recombinant vaccinia virus may express sPD-1, hyaluronidase, and/or IL-12 in a host cell.

Preferably, the recombinant vaccinia virus may comprise all of the sPD-1 gene, the hyaluronidase gene, and the IL-12 gene. That is, the recombinant vaccinia virus may be a vaccinia virus capable of expressing the sPD-1 gene, the hyaluronidase gene, and the IL-12 gene.

The aforementioned vaccinia virus may be a vaccinia virus having suppressed expression of any one selected from the group consisting of a gene encoding K3L, a gene encoding thymidine kinase (TK), a gene encoding vaccinia growth factor (VGF), and combinations thereof. Here, the combinations may refer to at least two of the gene encoding K3L, the gene encoding TK, and the gene encoding VGF.

For example, the recombinant vaccinia virus may be a vaccinia virus having the hyaluronidase gene and the IL-12 gene, or a vaccinia virus having the sPD-1 gene, the hyaluronidase gene, and the IL-12 gene,

in which expression of at least one of the VGF, TK, and K3L genes is suppressed, and expression of at least one of the sPD1-Fc, PH20, and IL-12 genes is induced.

In addition, variants of Tashkent vaccinia virus may include Tashkent vaccinia viruses in which expression of at least one of the VGF, TK, and K3L genes is suppressed, and expression of at least one of the sPD1-Fc, PH20, and IL-12 genes is induced.

In addition, variants of IHD-J vaccinia virus may include IHD-J vaccinia viruses in which expression of at least one of the VGF, TK, and K3L genes is suppressed, and expression of at least one of the sPD1-Fc, PH20, and IL-12 genes is induced.

Furthermore, variants of IHD-W vaccinia virus may include IHD-W vaccinia viruses in which expression of at least one of the VGF, TK, and K3L genes is suppressed, and expression of at least one of the sPD1-Fc, PH20, and IL-12 genes is induced.

In another aspect, there is provided a pharmaceutical composition for treating cancer, comprising, as an active ingredient, the recombinant vaccinia virus. Here, as described above, the recombinant vaccinia virus is a vaccinia virus in which expression of the sPD1-Fc and PH20 is induced. The expression of the VGF, TK, or K3L gene, or combinations thereof may be suppressed. The sPD1-Fc, PH20, IL-12, VGF, TK, and K3L genes are as described above.

The term "cancer" as used herein may be solid cancer or blood cancer. Here, the solid tumor may be selected from the group consisting of lung cancer, colorectal cancer, prostate cancer, thyroid cancer, breast cancer, brain cancer, head and neck cancer, fibrosarcoma, esophageal cancer, skin cancer, thymic cancer, gastric cancer, colon cancer, liver cancer, ovarian cancer, uterine cancer, bladder cancer, rectal cancer, gallbladder cancer, biliary tract cancer, pancreatic cancer, and combinations thereof. According to an embodiment, the cancer may be lung cancer, liver cancer, prostate cancer, head and neck cancer, fibrosarcoma, brain cancer, breast cancer, ovarian cancer,

Claims

[Claim 1]

A recombinant vaccinia virus, comprising:

a gene encoding soluble programmed cell death protein-1 (sPD-1) and a gene encoding hyaluronidase.

[Claim 2]

The recombinant vaccinia virus of claim 1, wherein the sPD-1 comprises the amino acid sequence of SEQ ID NO: 131 or SEQ ID NO: 133.

[Claim 3]

The recombinant vaccinia virus of claim 1, wherein the gene encoding sPD-1 comprises the nucleotide sequence of SEQ ID NO: 132 or SEQ ID NO: 134.

[Claim 4]

The recombinant vaccinia virus of claim 1, wherein the hyaluronidase comprises the amino acid sequence of SEQ ID NO: 135.

[Claim 5]

The recombinant vaccinia virus of claim 1, wherein the gene encoding hyaluronidase comprises the nucleotide sequence of SEQ ID NO: 136.

[Claim 6]

The recombinant vaccinia virus of claim 1, further comprising:

a gene encoding interleukin (IL)-12.

[Claim 7]

The recombinant vaccinia virus of claim 6, wherein the IL-12 comprises the amino acid sequence of SEQ ID NO: 137.

[Claim 8]

The recombinant vaccinia virus of claim 6, wherein the gene encoding IL-12 comprises any one nucleotide sequence of SEQ ID NO: 138 to SEQ ID NO: 140.

[Claim 9]

The recombinant vaccinia virus of claim 1, wherein the vaccinia virus has suppressed expression of any one selected from the group consisting of a gene encoding K3L, a gene encoding thymidine kinase (TK), a gene encoding vaccinia growth factor (VGF), and combinations thereof.

[Claim 10]

The recombinant vaccinia virus of claim 1, wherein the vaccinia virus is any one selected from the group consisting of Western Reserve (WR), New York Vaccinia Virus (NYVAC), Wyeth (The New York City Board of Health), LC16m8, Lister, Copenhagen, Tian Tan, USSR, Tashkent, Evans, International Health Division-J (IHD-J), International Health Division-White (IHD-W), variants thereof, and combinations thereof.

[Claim 11]

The recombinant vaccinia virus of claim 1, wherein the vaccinia virus is IHD-W.

[Claim 12]

A pharmaceutical composition for use in treating cancer, the pharmaceutical

composition comprising as an active ingredient the recombinant vaccinia virus of any one of claims 1 to 11.

[Claim 13]

The pharmaceutical composition of claim 12, wherein the cancer is solid cancer or blood cancer.

[Claim 14]

The pharmaceutical composition of claim 13, wherein the solid cancer is any one selected from the group consisting of lung cancer, colorectal cancer, prostate cancer, thyroid cancer, breast cancer, brain cancer, head and neck cancer, esophageal cancer, skin cancer, thymic cancer, gastric cancer, colon cancer, liver cancer, ovarian cancer, uterine cancer, bladder cancer, rectal cancer, gallbladder cancer, biliary tract cancer, pancreatic cancer, and combinations thereof.

[Claim 15]

The pharmaceutical composition of claim 13, wherein the blood cancer is any one selected from the group consisting of lymphoma, acute leukemia, multiple myeloma, and combinations thereof.

[Claim 16]

Use of the recombinant vaccinia virus of any one of claims 1 to 11, as an active ingredient, in the manufacture of a pharmaceutical composition for treating cancer.

[Claim 17]

The use of claim 16, wherein the cancer is solid cancer or blood cancer.

[Claim 18]

The use of claim 17, wherein the solid cancer is any one selected from the group consisting of lung cancer, colorectal cancer, prostate cancer, thyroid cancer, breast cancer, brain cancer, head and neck cancer, esophageal cancer, skin cancer, thymic cancer, gastric cancer, colon cancer, liver cancer, ovarian cancer, uterine cancer, bladder cancer, rectal cancer, gallbladder cancer, biliary tract cancer, pancreatic cancer, and combinations thereof.

[Claim 19]

The use of claim 17, wherein the blood cancer is any one selected from the group consisting of lymphoma, acute leukemia, multiple myeloma, and combinations thereof.