based on these vaccinia viruses. Vaccinia virus strains such as Western Reserve(WR), NYVAC, Wyeth, and Lister are also being developed as oncolytic viruses.

Aspects of the present disclosure may provide a recombinant vaccinia virus in which the expression of some genes is suppressed, and an anticancer composition containing the recombinant vaccinia virus as an active ingredient.

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

The present disclosure provides, as specified by the claims, a recombinant vaccinia virus in which expression of K3L, thymidine kinase (TK), and vaccinia growth factor (VGF) genes is suppressed.

The present specification describes a pharmaceutical composition for preventing or treating cancer which contains the recombinant vaccinia virus as an active ingredient.

The present specification describes a method for preventing or treating cancer, comprising a step of administering the recombinant vaccinia virus to an individual.

Advantageous Effects

The recombinant vaccinia virus as disclosed herein may selectively kill cancer cells and may exhibit an excellent replication ability in cancer cells. In addition, due to having an excellent cancer cell-selective killing ability, the recombinant vaccinia virus may have an advantage of being safer for use in the human body. Therefore, the recombinant vaccinia virus of the present disclosure can be usefully used as a composition for treating cancer.

Brief Description of Drawings

Fig. 1 is a schematic diagram showing a part of a construct of a shuttle plasmid

which suppresses the expression of VGF gene of the present disclosure.

Fig. 2 is a schematic diagram showing a part of a construct of a shuttle plasmid which suppresses the expression of TK gene of the present disclosure.

Fig. 3 is a schematic diagram showing a part of a construct of a shuttle plasmid which suppresses the expression of K3L gene of the present disclosure.

Fig. 4A shows results which identify that various cancer cell lines as shown in Table 1-1 are killed by a recombinant virus in which expression of VGF, TK, and K3L genes is suppressed.

[Table 1-1]

Carcinoma	Cell line
Lung cancer	A549
Brain cancer	U-87MG
Breast cancer	T-47D
Ovarian cancer	A2780
Pancreatic cancer	MIA PaCa-2
Colorectal cancer	SW620

Fig. 4B shows results which identify that various cancer cell lines as shown in Table 1-2 are killed by the recombinant virus in which expression of VGF, TK, and K3L genes is suppressed.

[Table 1-2]

Carcinoma	Cell line
Liver cancer	Hep3B
Prostate cancer	DU145
Head and neck cancer	FaDu
Fibrosarcoma	HT-1080

Fig. 5 shows results which identify that a recombinant IHD-W vaccinia virus in which VGF, TK, and K3L genes are deleted or inactivated and expression of the genes is suppressed induces death of a colorectal cancer cell line. The meanings of abbreviations for the deleted genes are as shown in Table 2:

[Table 2]

Abbreviation	Meaning
VTK	All of VGF, TK, and K3L genes are deleted
ViTK	Expression of VGF gene is inactivated, and both TK and K3L genes are deleted
VTiK	Expression of TK gene is inactivated, and both VGF and K3L genes are deleted
VTKi	Expression of K3L gene is inactivated, and both VGF and TK genes are deleted

Fig. 6 is a graph which identifies a killing ability of a recombinant vaccinia virus, in which expression of K3L only or, both VGF and TK, or all VGF and TK and K3L genes being suppressed, against cancer cells relative to normal cells:

(a) is a graph obtained by making a comparison for a killing ability of a recombinant IHD-W-K, IHD-W-VT or IHD-W-VTK vaccinia virus against cancer cells relative to normal cells, based on a IHD-W-VTK value; and (b) is a graph obtained by making a comparison for a killing ability of a recombinant WR-ViTi or WR-ViTiKi vaccinia virus against cancer cells relative to normal cells, based on a WR-ViTiKi value.

Fig. 7 is a graph obtained by observing changes in tumor size after administration of a recombinant vaccinia virus, in which expression of both VGF and TK or all VGF and TK and K3L genes being suppressed, to a colorectal cancer mouse model:

(a) is a graph obtained by observing changes in tumor size after administration of a recombinant IHD-W-VT or IHD-W-VTK vaccinia virus to a colorectal cancer mouse model; and (b) is a graph obtained by observing changes in tumor size after administration of a recombinant WR-ViTi or WR-ViTiKi vaccinia virus to a colorectal cancer mouse model.

Fig. 8 is a graph which identifies changes in body weight of mice on an individual basis after administration of a recombinant vaccinia virus, in which expression of both VGF and TK or all VGF and TK and K3L genes being suppressed, to a colorectal cancer mouse model:

(a) is a graph which identifies changes in body weight of mice on an individual basis after administration of a recombinant IHD-W-VT or IHD-W-VTK vaccinia virus to a colorectal cancer mouse model; and (b) is a graph which identifies changes in body weight of mice on an individual basis after administration of a recombinant WR-ViTi or WR-ViTiKi vaccinia virus to a colorectal cancer mouse model.

Fig. 9 is a graph which identifies a mortality rate of mice after administration of a recombinant vaccinia virus, in which expression of both VGF and TK or all VGF and TK and K3L genes being suppressed, to a colorectal cancer mouse model:

(a) is a graph which identifies a mortality rate of mice after administration of a recombinant IHD-W-VT or IHD-W-VTK vaccinia virus to a colorectal cancer mouse model; and (b) is a graph which identifies a mortality rate of mice after administration of a recombinant WR-ViTi or WR-ViTiKi vaccinia virus to a colorectal cancer mouse model.

Fig.10 shows results which identify inflammation reaction in tails of mice after administration of a recombinant IHD-W vaccinia virus, in which expression of both VGF and TK or all VGF and TK and K3L genes being suppressed, to a colorectal cancer mouse model:

(a) shows results which identify inflammatory response in tails of mice to which a recombinant IHD-W-VT vaccinia virus was administered, and (b) shows results of confirming inflammatory reaction in tails of mice to which a recombinant IHD-W-VTK vaccinia virus was administered.

Detailed Description of Invention

Hereinafter, the present invention will be described in detail and by way of example only.

In an aspect of the present disclosure, there is provided a recombinant vaccinia virus in which expression of VGF, TK, and K3L genes is suppressed.

The term “VGF” as used herein means vaccinia growth factor. The vaccinia growth factor is an enzyme exhibiting a similar activity to epithelial growth factor. The vaccinia growth factor encoded by the VGF gene exhibits a growth factor activity in the case of being infected with the virus and can be synthesized at an initial stage of infection caused by the virus. The VGF may be a sequence of GenBank: AAO89288.1, ABD52455.1, or AIX98927.1, but is not limited thereto. Specifically, the VGF may be a base sequence encoding an amino acid sequence represented by SEQ ID NO: 67, and the VGF gene may be a base sequence represented by SEQ ID NO: 66. The VGF or a gene thereof may have a homology of about 70% or 75% or more, and preferably about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%,

or 89% or more, to the amino acid sequence of SEQ ID NO: 67 or the base sequence of SEQ ID NO: 66. In addition, the VGF or a gene thereof may have a

homology of about 90%, 91%, 92%, 93%, or 94% or more, preferably about 95%, 96%, 97%, 98%, or 99% or more, and most preferably about 99% or more, to the amino acid sequence of SEQ ID NO: 67 or the base sequence of SEQ ID NO: 66.

The term "TK" as used herein means thymidine kinase. The thymidine kinase is an enzyme involved in the biosynthesis of nucleotides. The thymidine kinase encoded by the TK gene causes a phosphoric acid at a γ position of ATP to bind to thymidine so that nucleotides constituting a viral DNA can be produced. The TK may be a sequence of GenBank: AAO89373.1, ABD52560.1, or AIX99011.1, but is not limited thereto. Specifically, the TK may be a base sequence encoding an amino acid sequence represented by SEQ ID NO: 69, and the TK gene may be a base sequence represented by SEQ ID NO: 68. The TK or a gene thereof may have a homology of about 70% or 75% or more, and preferably about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, or 89% or more, to the amino acid sequence of SEQ ID NO: 69 or the base sequence of SEQ ID NO: 68. In addition, the TK or a gene thereof may have a homology of about 90%, 91%, 92%, 93%, or 94% or more, preferably about 95%, 96%, 97%, 98%, or 99% or more, and most preferably about 99% or more, to the amino acid sequence of SEQ ID NO: 69 or the base sequence of SEQ ID NO: 68.

The term "K3L" as used herein means K3L protein. The K3L protein encoded by the K3L gene is a protein having homology to translation initiation factor-2α (eIF-2α) and can suppress an action of protein kinase R (PKR) which is an interferon activator. The K3L may be a sequence of GenBank: AAO89313.1, ABD52483.1, or AGB75754.1, but is not limited thereto. Specifically, the K3L may have a base sequence encoding an amino acid sequence represented by SEQ ID NO: 71, and the K3L gene may be a base sequence represented by SEQ ID NO: 70. The K3L or a gene thereof may have a homology of about 70% or 75% or more, and preferably about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, or 89% or more, to the amino acid sequence of SEQ ID NO:. 71 or the base sequence of SEQ ID NO: 70. In addition, the K3L or a gene thereof may have a homology of about 90%, 91%, 92%, 93%, or 94% or more, preferably about 95%, 96%, 97%, 98%, or 99% or more, and most preferably about 99% or more, to the amino acid sequence of SEQ ID NO: 71 or the base sequence of

SEQ ID NO: 70.

Suppressed expression of a gene according to the present disclosure means that the gene is not expressed or only a part of the gene is expressed by partial or entire deletion of the gene or insertion of a foreign gene into the gene so that an activity of a protein encoded by the gene is not exhibited. A method for deleting the gene or inserting a foreign gene can be performed by a method well known in the art. For example, this can be performed by methods for inserting a foreign gene which is disclosed in Molecular Cloning, A Laboratory Manual, Second Edition, by J. Sambrook, E. F. Fritsch and T. Maniatis (2003), Cold Spring Harbor Laboratory Press, Virology Methods Manual, edited by Brian W J Mahy and Hillar O Kangro (1996) Academic Press and Expression of genes by Vaccinia virus vectors, and Current Protocols in Molecular Biology, published by John Wiley and Son (1998), Chapter 16. In an exemplified instance, a foreign gene was inserted using pGEM-T Easy (Promega, Cat No. A1360) or pGEM-T (Promega, Cat No. A3600) vector system.

The vaccinia virus may be selected from the group consisting of Western Reserve(WR), New York Vaccinia Virus (NYVAC), Wyeth (The New York City Board of Health; NYCBOH), LC16m8, Lister, Copenhagen, Tian Tan, USSR, TashKent, Evans, International Health Division-J (IHD-J), International Health Division-White (IHD-W), and variants thereof, but is not limited thereto. Specifically, the vaccinia virus may be WR, Lister, or IHD-W vaccinia virus, and may have a sequence of GenBank: AY243312.1, DQ121394.1, or AIX98951.1. In an embodiment of the present invention, the vaccinia virus may be IHD-W.

The term “V” or “virus V” as used herein means a recombinant vaccinia virus in which VGF which is a vaccinia growth factor gene is deleted, and the virus does not express VGF gene due to deletion of the VGF gene.

In addition, the term “Vi” or “virus Vi” as used herein means a recombinant vaccinia virus in which expression of vaccinia growth factor is inactivated, and the virus does not express VGF gene. Expression of the vaccinia growth factor can be suppressed by inserting a foreign gene into the VGF gene.

In addition, the term “T” or “virus T” as used herein means a recombinant vaccinia virus in which thymidine kinase (TK) gene is deleted, and the virus does not express the TK gene due to deletion of the TK gene.

In addition, the term “Ti” or “virus Ti” as used herein means a recombinant vaccinia virus in which expression of thymidine kinase is inactivated, and the virus does not express TK gene. Expression of the thymidine kinase can be suppressed by inserting a foreign gene into the TK gene.

In addition, the term “K” or “virus K” as used herein means a recombinant vaccinia virus in which K3L gene is deleted, and the virus does not express the K3L gene due to deletion of the K3L gene.

In addition, the term “Ki” or “virus Ki” as used herein means a recombinant vaccinia virus in which expression of K3L gene is inactivated, and the virus does not express K3L. Expression of the K3L protein can be suppressed by inserting a foreign gene into the K3L gene.

In addition, the term “VT” or “virus VT” as used herein means a recombinant vaccinia virus in which VGF and TK genes are deleted. In addition, the term “ViTi” or “virus ViTi” as used herein means a recombinant vaccinia virus in which expression of vaccinia growth factor and thymidine kinase are inactivated. Methods for inactivating expression of the vaccinia growth factor and thymidine kinase are as described above.

In addition, the term “VTK” or “virus VTK” as used herein means a recombinant vaccinia virus in which VGF, TK, and K3L genes are deleted. In addition, the term “ViTiKi” or “virus ViTiKi” as used herein means a recombinant vaccinia virus in which expression of vaccinia growth factor, thymidine kinase, and K3L protein are inactivated. Methods for inactivating expression of the vaccinia growth factor, thymidine kinase, and K3L protein are as described above.

In addition, the term “ViTK” or “virus ViTK” as used herein means a recombinant vaccinia virus in which expression of vaccinia growth factor is inactivated, and TK and K3L genes are deleted. In addition, the term “VTiK” or “virus VTiK” as used herein means a recombinant vaccinia virus in which expression of thymidine kinase is inactivated, and VGF and K3L genes are deleted. In addition, the term “VTKi” or “virus VTKi” as used herein means a recombinant vaccinia virus in which expression of K3L protein is inactivated, and VGF and TK genes are deleted.

In addition, the present specification describes a pharmaceutical composition

expression of VTK gene is suppressed have an anticancer activity (Fig.5). In addition, in a case where normal cells and cancer cells are treated with recombinant IHD-W-K, IHD-W-VT, IHD-W-VTK, WR-K, WR-ViTi, and WR-ViTiKi vaccinia viruses, it was identified that the recombinant IHD-W-VTK or WR-ViTiKi vaccinia virus in which expression of VGF, TK, and K3L genes is simultaneously suppressed exhibits a relatively superior killing ability against cancer cells relative to normal cells as compared to the recombinant IHD-W-K or WR-K vaccinia virus in which the only expression of K3L gene is suppressed or the recombinant IHD-W-VT or WR-ViTi vaccinia virus in which expression of VGF and TK genes are simultaneously suppressed (Fig.6).

In addition, the recombinant IHD-W-VT and IHD-W-VTK vaccinia viruses and the recombinant WR-ViTi and WR-ViTiKi vaccinia viruses were administered to a tumor mouse model. As a result, it was identified that all of the viruses suppressed cancer growth (Fig.7).

In addition, it was identified that a tumor mouse model to which the recombinant IHD-W-VTK or WR-ViTiKi vaccinia virus was administered exhibited lower weight loss and mortality rate than a tumor mouse model to which the recombinant IHD-W-VT or WR-ViTi vaccinia virus was administered (Figs. 8 and 9). In addition, it was identified that mice to which the recombinant IHD-W-VTK vaccinia virus was administered exhibited a less inflammatory response in a tail region than mice to which the recombinant IHD-W-VT vaccinia virus was administered.

Accordingly, a pharmaceutical composition of the present disclosure for preventing or treating cancer which contains, as an active ingredient, a recombinant vaccinia virus in which expression of K3L, TK, and VGF genes is suppressed can be usefully used for preventing or treating cancer.

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. In one instance, cancer may be lung cancer, liver cancer, prostate cancer, head and neck cancer, fibrosarcoma, brain cancer, breast cancer, ovarian cancer, pancreatic cancer, or colorectal cancer. In addition, the blood cancer

may be selected from the group consisting of lymphoma, acute leukemia, multiple myeloma, and combinations thereof.

The pharmaceutical composition may further contain one or more pharmaceutically acceptable additives selected from the group consisting of excipients, lubricants, wetting agents, sweeteners, fragrances, and preservatives.

The composition may be formulated according to a conventional method. The composition can be formulated employing a method known in the art so as to provide rapid, sustained, or delayed the release of an active ingredient, in particular after being administered to a mammal. According to the formulation, the composition can be appropriately administered to an individual. Such administration may be parenteral administration, and examples thereof can include intra-cancer tissue, intradermal, intramuscular, intraperitoneal, intravenous, intraarterial, subcutaneous, intranasal, epidural, and oral route. A form of preparation for parenteral administration may be an injectable preparation.

The present specification provides a method for preventing or treating cancer, comprising a step of administering the recombinant vaccinia virus to an individual.

The individual may be a mammal, in particular, a human. The composition can be appropriately administered by a person skilled in the art depending on the patient's age, sex, weight, the severity of disease symptom, and route of administration. The administration may be once a day or several times a day.

A preferred dosage of the recombinant vaccinia virus varies depending on condition and body weight of an individual, severity of disease, drug form, route of administration, and period, and can be appropriately selected by a person skilled in the art. Specifically, the dosage may be such that a patient receives virus particles, virus units having infectivity ($TCID_{50}$), or plaque forming units (pfu) of 1×10^5 to 1×10^{18}, and preferably 1×10^5, 2×10^5, 5×10^5, 1×10^6, 2×10^6, 5×10^6, 1×10^7, 2×10^7, 5×10^7, 1×10^8, 2×10^8, 5×10^8, 1×10^9, 2×10^9, 5×10^9, 1×10^{10}, 5×10^{10}, 1×10^{11}, 5×10^{11}, 1×10^{12}, 1×10^{13}, 1×10^{14}, 1×10^{15}, 1×10^{16}, 1×10^{17} or more, in which various values and ranges therebetween can be included. In addition, a dosage of the virus may be 0.1 ml, 1 ml, 2 ml, 3 ml, 4 ml, 5 ml, 6 ml, 7 ml, 8 ml,

9 ml, 10 ml or more, and all values and ranges therebetween can be included.

The following examples are intended to illustrate the present invention, and the present invention is not limited thereto.

I. Production of recombinant vaccinia virus

The present inventors constructed recombinant vaccinia virus vectors in which thymidine kinase (TK), vaccinia growth factor (VGF), and K3L genes are deleted or expression thereof is inactivated. Using these vectors, recombinant vaccinia viruses in which expression of the above genes is suppressed were produced and comparison was made for properties thereof as anti-cancer substances.

Example 1. Production of recombinant WR vaccinia virus

Example 1.1. Construction of recombinant WR vaccinia virus vector in which VGF, TK, and K3L genes are inactivated or deleted

Example 1.1.1. Construction of recombinant WR vaccinia virus vector in which expression of VGF gene is inactivated

Genes that flank VGF gene on both sides in the genomic DNA of WR vaccinia virus (ATCC, Cat No. VR-1354) were amplified by PCR and inserted into pGEM-T Easy, respectively, to construct pGEM-T Easy-VGF-L(WR) and pGEM-T Easy-VGF-R(WR). Information on primers used for the amplification of homologous base sequences that flank the VGF gene on both sides is shown in Table 3.

[Table 3]

Name	Sequence (5'→3')	SEQ ID NO
VGF-L forward (WR)	CGCAGCTGTGTTATCGATTGATAGTGGTGTCCT	SEQ ID NO: 1
VGF-L reverse (WR)	CTGCAGCGCTAGCACCGCATAATCTGATAGCTGGAATA	SEQ ID NO: 2
VGF-R forward (WR)	CGGGATCCGTTAATTAAACTCGACGAACTAAACTACCTATAC	SEQ ID NO: 3
VGF-R reverse (WR)	CGATATCGGAAAATGTCTGTTAGTAAATAACCATC	SEQ ID NO: 4

Example 1.1.4. Construction of recombinant WR vaccinia virus vector in which expression of K3L gene is inactivated

A gene that flanks K3L gene on the left side and a part of the K3L gene in the genomic DNA of WR vaccinia virus were amplified by PCR. Here, the amplification was carried out with the start codon of the K3L gene being placed immediately after the K3L-L sequence, and primers used for the amplification of the homologous sequence on the left side of the K3L gene are shown in Table 6. Here, a K3L-L-K3Li(WR) fragment which was amplified and includes a part that excludes and follows the start codon of the K3L gene was obtained and then ligated with a pGEM-T Easy vector, to construct pGEM-T Easy-K3L-L-K3Li(WR).

[Table 6]

Name	Sequence (5'→3')	SEQ ID NO
K3L-Li forward	TGTACGTATATTTAGATGTTTTCAGCT	SEQ ID NO: 31
K3L-Li reverse	ATAAGCTTCTTGCATTTTGTTATTCGT	SEQ ID NO: 32
K3L-Ri forward	CGCAGATAAAAACATATCCTTGTTAAC	SEQ ID NO: 33
K3L-Ri reverse	GTTAACAAGGATATGTTTTTATCTGCG	SEQ ID NO: 34

The WR K3L shuttle plasmid and pGEM-T Easy-K3L-L-K3Li(WR) as constructed in Example 1.1.3 were treated with SnaBI and HindIII, and ligated to construct pSP72-K3L-L-K3Li-p7.5-DsRed--TF-K3L-R(WR). In order to introduce the start codon of K3L into the constructed pSP72-K3L-L-K3Li-p7.5-DsRed--TF-K3L-R(WR), a point mutation was performed using primers as shown in Table 6, so that pSP72-K3L-L-K3Li-p7.5-DsRed-TF-$K3L_{ATG}$-K3L-R(WR) (hereinafter referred to as "WR K3L(i) shuttle plasmid") was finally constructed.

Example 1.2. Production of recombinant WR vaccinia virus in which VGF, TK, and K3L genes are deleted or inactivated

Example 1.2.1. Production of WR vaccinia virus in which K3L gene is deleted

In order to secure a recombinant virus, HeLa (ATCC, Cat No. CCL-2) cells were prepared in a 6-well plate at a condition of 3×10^5 cells/well and in a state of MEM medium containing 2% fetal bovine serum. Then, the HeLa cells were transfected with 2 μg of the WR K3L shuttle plasmid as constructed in Example 1.1.3 using jetPRIME (Polyplus, Cat No. 114-07) and simultaneously treated with 0.05 MOI of WR wild-type vaccinia virus. After 2

incubator under a condition of 37°C and 5% CO_2, and then aliquoted into 96-well plates.

[Table 14]

Carcinoma	Cell line	Medium used
Brain cancer	U-87MG (ATCC, HTB-14)	MEM medium containing 10% fetal bovine serum
Liver cancer	Hep3B (ATCC, HB-8064)	
Prostate cancer	DU145 (ATCC, HTB-81)	
Head and neck cancer	FaDu (ATCC, HTB-43)	
Fibrosarcoma	HT-1080 (KCLB, 10121)	
Breast cancer	T-47D (ATCC, HTB-133)	RPMI medium containing 10% fetal bovine serum and recombinant insulin
Pancreatic cancer	MIA PaCa-2 (KCLB, 21420)	DMEM medium containing 10% fetal bovine serum
Colorectal cancer	SW620 (KCLB, 60068)	RPMI medium containing 10% fetal bovine serum
Ovarian cancer	A2780 (Sigma-Aldrich, 93112519)	
Lung cancer	A549 (ATCC, Cat No. CCL-185)	

Here, aliquoting was carried out such that the number of cells per well was 5×10^4 for SW620, 2×10^4 for A2780, A549, DU145, T-47D, and FaDu, 1×10^4 for Hep3B and HT-1080, and 5×10^3 for MIA PaCa-2 and U-87 MG. After 24 hours of the incubation, the cell lines were infected with the recombinant IHD-W vaccinia virus VTK, the recombinant WR vaccinia virus ViTiKi, or the recombinant Lister vaccinia virus VTK so that 0.5 MOI was achieved for each virus. Here, cells which had not been treated with a virus were used as a control group. After 3 to 5 days, the cells were stained with CCK-8 (Dojindo, Cat No. CK04) solution to identify survival rates of the cancer cell lines. The results are shown in Figs. 4A and 4B.

As shown in Fig.4, it was identified that in a case where the VGF, TK, and K3L genes are deleted or expression thereof is inactivated, a killing ability against various types of cancer cells was exhibited regardless of a strain of vaccinia.

Experimental Example 2. Identification of cancer cell-killing ability of recombinant vaccinia virus in which VGF, TK, and K3L genes are deleted or expression thereof is inactivated

In order to identify whether the genes of the present disclosure whose expression is suppressed in a recombinant vaccinia virus exhibit a different killing ability against cancer cells depending on methods of suppressing expression thereof, a degree of death of the

CLAIMS

1. A recombinant vaccinia virus in which expression of K3L, thymidine kinase (TK), and vaccinia growth factor (VGF) genes is suppressed.

2. The recombinant vaccinia virus of claim 1, wherein the expression of the genes is suppressed by partial or entire deletion of the genes, or the insertion of a foreign gene into the genes.

3. The recombinant vaccinia virus of any preceding claim, wherein the VGF gene is a polynucleotide consisting of the base sequence of SEQ ID NO: 66.

4. The recombinant vaccinia virus of any preceding claim, wherein the TK gene is a polynucleotide consisting of the base sequence of SEQ ID NO: 68.

5. The recombinant vaccinia virus of any preceding claim, wherein the K3L gene is a polynucleotide consisting of the base sequence of SEQ ID NO: 70.

6. The recombinant vaccinia virus of any preceding claim, 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), and variants thereof.

7. The recombinant vaccinia virus of claim 6, wherein the vaccinia virus is IHD-W.

8. A pharmaceutical composition comprising the recombinant vaccinia virus of any preceding claim as an active ingredient.

9. The recombinant vaccinia virus of any of claims 1 to 7 for use in the prevention or treatment of cancer.

10. Use of the recombinant vaccinia virus of any of claims 1 to 7 in the manufacture of a medicament for the prevention or treatment of cancer.

11. Use of the recombinant vaccinia virus of any of claims 1 to 7 in the manufacture of a pharmaceutical composition for preventing or treating cancer.

12. The recombinant vaccinia virus for use according to claim 9, or the use of the recombinant vaccinia virus according to claim 10 or claim 11, wherein the cancer is solid cancer or blood cancer.

13. The recombinant vaccinia virus for use according to claim 12, or the use of the recombinant vaccinia virus according to claim 12, 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.

14. The recombinant vaccinia virus for use according to claim 12, or the use of the recombinant vaccinia virus according to claim 12, wherein the blood cancer is any one selected from the group consisting of lymphoma, acute leukemia, multiple myeloma, and combinations thereof.