SUMMARY

[0005a] In one aspect, provided herein is use of a therapeutically effective amount of an oncolytic virus in the manufacture of a first medicament, and a nucleocytoplasmic transport inhibitor in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating cancer, wherein the first and second medicaments are to be administered to a subject.

[0006] Disclosed herein, in some ~~aspect~~examples, is a method of treating cancer, comprising administering to a subject a therapeutically effective amount of an oncolytic virus, and a nucleocytoplasmic transport inhibitor.

[0007] In some ~~embodiment~~examples, the oncolytic virus is derived from the Poxviridae family. In some ~~embodiment~~examples, the oncolytic virus is derived from Chordopoxvirinae subfamily or Entomopoxvirinae subfamily. In some ~~embodiment~~examples, the oncolytic virus is derived from a virus genus of Orthopoxvirus, Cervidpoxvirus, Parapoxvirus, Avipoxvirus, Capripoxvirus, Leporipoxvirus, Suipoxvirus, Molluscipoxvirus, Yatapoxvirus, Alphaentomopoxvirus, Betaentomopoxvirus, or Gammaentopoxvirus. In some ~~embodiment~~examples, the oncolytic virus is derived from genus Leporipoxvirus. In some ~~embodiment~~examples, the oncolytic virus is a myxoma virus (MYXV). In some ~~embodiment~~examples, the oncolytic virus is derived from genus Orthopoxvirus. In some ~~embodiment~~examples, the virus is genetically modified. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is selected from the group consisting of Leptomycin A, Leptomycin B, Ratjadone A, Ratjadone B, Ratjadone C, Ratjadone D, Anguinomycin A, Goniothalamin, piperlongumine, plumbagin, curcumin, valtrate, acetoxychavicol acetate, prenylcoumarin osthol, KOS 2464, PKF050-638, CBS9106, and Selinexor. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is Leptomycin B. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is Selinexor. In some ~~embodiment~~examples, the cancer is a solid tumor. In some ~~embodiment~~examples, the solid tumor is a sarcoma or a carcinoma. In some ~~embodiment~~examples, the solid tumor is fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, uterine cancer, testicular cancer, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, schwannoma, meningioma, melanoma, neuroblastoma, or retinoblastoma. In some ~~embodiment~~examples, the solid tumor is colorectal adenocarcinoma, pancreatic cancer, or melanoma. In some ~~embodiment~~examples, the oncolytic virus and the nucleocytoplasmic transport

inhibitor are administered simultaneously. In some ~~embodiment~~examples, the oncolytic virus and the nucleocytoplasmic transport inhibitor are administered sequentially. In some ~~embodiment~~examples, the oncolytic virus is administered before administering the nucleocytoplasmic transport inhibitor. In some ~~embodiment~~examples, the oncolytic virus is administered after administering the nucleocytoplasmic transport inhibitor. In some ~~embodiment~~examples, the method comprises administering the oncolytic virus and the nucleocytoplasmic transport inhibitor for a period of at least 1 day, at least 2 days, at least 3 days, at least 1 week, at least 2 weeks, at least 3 weeks, at least 4 weeks, at least 1 month, at least 3 months, at least 6 months, or at least 1 year. In some ~~embodiment~~examples, the method comprises administering the oncolytic virus, the nucleocytoplasmic transport inhibitor, or both to the subject twice a week, once a week, once every two weeks, once every three weeks, once every four weeks, once a month, or once every two months. In some ~~embodiment~~examples, the oncolytic virus is administered locally to a cancer tissue to be treated. In some ~~embodiment~~examples, the oncolytic virus is administered by intratumoral injection. In some ~~embodiment~~examples, a multiplicity of infection (MOI) of the oncolytic virus for the tissue is from about 0.01 to about 10. In some ~~embodiment~~examples, a multiplicity of infection (MOI) of the oncolytic virus for the tissue is from about 0.05 to about 5. In some ~~embodiment~~examples, a concentration of the nucleocytoplasmic transport inhibitor at the tissue is from about 0.0001 μM to about 100 μM. In some ~~embodiment~~examples, a concentration of the nucleocytoplasmic transport inhibitor at the tissue is from about 0.01 μM to about 1 μM.

[0008] Disclosed herein, in some ~~aspect~~examples, is a method of killing a cancer cell comprising: contacting the cancer cell with an oncolytic virus and a nucleocytoplasmic transport inhibitor, thereby killing the cancer cell.

[0009] Disclosed herein, in some ~~aspect~~examples, is a method of enhancing susceptibility of a cancer cell to infection by an oncolytic virus, comprising contacting the cancer cell to an oncolytic virus and a nucleocytoplasmic transport inhibitor.

[0010] Disclosed herein, in some ~~aspect~~examples, is a method of inducing a cancer cell to be susceptible to infection by an oncolytic virus, comprising contacting the cancer cell to the oncolytic virus and a nucleocytoplasmic transport inhibitor.

[0011] Disclosed herein, in some ~~aspect~~examples, is a method of converting a nonpermissive cancer cell to a permissive cancer cell comprising contacting the nonpermissive cancer cell with an oncolytic virus and a nucleocytoplasmic transport inhibitor.

[0012] Disclosed herein, in some ~~aspect~~examples, is a method of increasing proliferation of an oncolytic virus in a cancer cell that is not susceptible to infection by the oncolytic virus comprising contacting the cancer cell to an oncolytic virus and a nucleocytoplasmic transport inhibitor.

[0013] In some ~~embodiment~~examples, the oncolytic virus is a virus from the Poxviridae family. In some ~~embodiment~~examples, the oncolytic virus is a virus from Chordopoxvirinae subfamily or

Entomopoxvirinae subfamily. In some ~~embodiment~~examples, the oncolytic virus is from a virus genus that is Orthopoxvirus, Cervidpoxvirus, Parapoxvirus, Avipoxvirus, Capripoxvirus, Leporipoxvirus, Suipoxvirus, Molluscipoxvirus, Yatapoxvirus, Alphaentomopoxvirus, Betaentomopoxvirus, or Gammaentopoxvirus. In some ~~embodiment~~examples, the oncolytic virus is from genus Leporipoxvirus. In some ~~embodiment~~examples, the oncolytic virus is a myxoma virus (MYXV). In some ~~embodiment~~examples, the oncolytic virus is from genus Orthopoxvirus. In some ~~embodiment~~examples, the virus is genetically modified. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is selected from the group consisting of Leptomycin A, Leptomycin B, Ratjadone A, Ratjadone B, Ratjadone C, Ratjadone D, Anguinomycin A, Goniothalamin, piperlongumine, plumbagin, curcumin, valtrate, acetoxychavicol acetate, prenylcoumarin osthol, KOS 2464, PKF050-638, CBS9106, and Selinexor. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is Leptomycin B. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is Selinexor. In some ~~embodiment~~examples, the cancer cell is colorectal cancer cell, pancreatic cancer cell, melanoma cancer cell. In some ~~embodiment~~examples, the cancer cell is a human cancer cell. In some ~~embodiment~~examples, the cancer cell is contacted to an oncolytic virus and a nucleocytoplasmic transport inhibitor in vivo. In some ~~embodiment~~examples, the cancer cell is contacted to an oncolytic virus and a nucleocytoplasmic transport inhibitor ex vivo. In some ~~embodiment~~examples, the method comprises contacting the cancer cell with the oncolytic virus and the nucleocytoplasmic transport inhibitor simultaneously. In some ~~embodiment~~examples, the method comprises contacting the cancer cell with the oncolytic virus and the nucleocytoplasmic transport inhibitor sequentially. In some ~~embodiment~~examples, the cancer cell is contacted with the oncolytic virus before being contacted with the nucleocytoplasmic transport inhibitor. In some ~~embodiment~~examples, the cancer cell is contacted with the nucleocytoplasmic transport inhibitor before being contacted with the oncolytic virus. In some ~~embodiment~~examples, the cancer cell is contacted with the oncolytic virus at a MOI of from about 0.01 to about 10. In some ~~embodiment~~examples, the cancer cell is contacted with the oncolytic virus at a MOI of from about 0.05 to about 5. In some ~~embodiment~~examples, the method comprises incubating the cancer cell in a media comprising the nucleocytoplasmic transport inhibitor at a concentration of from about 0.0001 μM to about 100 μM. In some ~~embodiment~~examples, the method comprises incubating the cancer cell in a media comprising the nucleocytoplasmic transport inhibitor at a concentration of from about 0.01 μM to about 1 μM. In some ~~embodiment~~examples, the method comprises contacting the cancer cell with a media comprising the nucleocytoplasmic transport inhibitor at a concentration of from about 0.0001 μM to about 100 μM. In some ~~embodiment~~examples, the method comprises contacting the cancer cell with a media comprising the nucleocytoplasmic transport inhibitor at a concentration of from about 0.01 μM to about 1 μM. In some ~~embodiment~~examples, the method further comprises contacting the oncolytic virus to an autologous or heterologous cell ex vivo. In some ~~embodiment~~examples, the autologous or

heterologous cell is a bone marrow cell or a macrophage cell. In some ~~embodiment~~examples, the method further comprises injecting the autologous or heterologous cell to the subject.

[0014] Disclosed herein, in some ~~aspect~~examples is a pharmaceutical composition comprising: an oncolytic virus, and a nucleocytoplasmic transport inhibitor.

[0015] In some ~~embodiment~~examples, the pharmaceutical composition further comprises a pharmaceutically acceptable excipient or carrier. In some ~~embodiment~~examples, the oncolytic virus is derived from the Poxviridae family. In some ~~embodiment~~examples, the oncolytic virus is derived from Chordopoxvirinae subfamily or Entomopoxvirinae subfamily. In some ~~embodiment~~examples, the oncolytic virus is derived from a virus genus of Orthopoxvirus, Cervidpoxvirus, Parapoxvirus, Avipoxvirus, Capripoxvirus, Leporipoxvirus, Suipoxvirus, Molluscipoxvirus, Yatapoxvirus, Alphaentomopoxvirus, Betaentomopoxvirus, or Gammaentopoxvirus. In some ~~embodiment~~examples, the oncolytic virus is derived from genus Leporipoxvirus. In some ~~embodiment~~examples, the oncolytic virus is a myxoma virus (MYXV). In some ~~embodiment~~examples, the oncolytic virus is derived from genus Orthopoxvirus. In some ~~embodiment~~examples, the virus is genetically modified. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is selected from the group consisting of Leptomycin A, Leptomycin B, Ratjadone A, Ratjadone B, Ratjadone C, Ratjadone D, Anguinomycin A, Goniothalamin, piperlongumine, plumbagin, curcumin, valtrate, acetoxychavicol acetate, prenylcoumarin osthol, KOS 2464, PKF050-638, CBS9106, and Selinexor. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is Leptomycin B. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is Selinexor. In some ~~embodiment~~examples, the pharmaceutical composition is in a unit dosage form suitable for intratumoral or parenteral administration. In some ~~embodiment~~examples, the unit dosage comprises from about $1x10^3$ plaque-forming units (PFU) to about $1x10^{10}$ PFU of the oncolytic virus per mL. In some ~~embodiment~~examples, the unit dosage comprises from about $1x10^5$ PFU to about $1x10^{10}$ PFU of the oncolytic virus per mL. In some ~~embodiment~~examples, a weight ratio between the oncolytic virus and the nucleocytoplasmic transport inhibitor is from about $1x10^9$ to about $1x10^{-9}$.

[0016] Some ~~embodiment~~examples relate to a method of treating cancer, comprising administering to a subject a therapeutically effective amount of an oncolytic virus, and a nucleocytoplasmic transport inhibitor. In one ~~aspect~~example, described herein is a method of killing a cancer cell comprising: contacting a cancer cell with a therapeutically effective amount of an oncolytic virus and a nucleocytoplasmic transport inhibitor, thereby killing said cancer cell. In one ~~aspect~~example, described herein is a method of enhancing susceptibility of a cancer cell to infection by an oncolytic virus, comprising: contacting the cancer cell to an oncolytic virus and a nucleocytoplasmic transport inhibitor. In one ~~aspect~~example, described herein is a method of making a cancer cell susceptible to infection by an oncolytic virus, comprising contacting the cancer cell to the oncolytic virus and a nucleocytoplasmic transport inhibitor. In one ~~aspect~~example, described herein is a method of converting a nonpermissive cancer cell to a permissive cancer cell comprising: contacting the nonpermissive cancer cell to an oncolytic virus to a therapeutically effective amount of said oncolytic virus and a

nucleocytoplasmic transport inhibitor. In one ~~aspect~~example, described herein is a method of increasing proliferation of an oncolytic virus in a cancer cell that is not susceptible to infection by the oncolytic virus, comprising: contacting the cancer cell to an oncolytic virus and a nucleocytoplasmic transport inhibitor. In some ~~embodiment~~examples, the oncolytic virus is a virus from the *Poxviridae* family. In some ~~embodiment~~examples, the oncolytic virus is a virus from *Chordopoxvirinae* subfamily or *Entomopoxvirinae* subfamily. In some ~~embodiment~~examples, the oncolytic virus is from a virus genus that is *Orthopoxvirus*, *Cervidpoxvirus*, *Parapoxvirus*, *Avipoxvirus*, *Capripoxvirus*, *Leporipoxvirus*, *Suipoxvirus*, *Molluscipoxvirus*, *Yatapoxvirus*, *Alphaentomopoxvirus*, *Betaentomopoxvirus*, or *Gammaentopoxvirus*. In some ~~embodiment~~examples, the oncolytic virus is from genus *Leporipoxvirus*. In some ~~embodiment~~examples, the oncolytic virus is a *myxoma virus* (MYXV). In some ~~embodiment~~examples, the oncolytic virus is from genus *Orthopoxvirus*. In some ~~embodiment~~examples, the virus is genetically modified. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is selected from the group consisting of Leptomycin A, Leptomycin B, Ratjadone A, Ratjadone B, Ratjadone C, Ratjadone D, Anguinomycin A, Goniothalamin, piperlongumine, plumbagin, curcumin, valtrate, acetoxychavicol acetate, prenylcoumarin osthol, KOS 2464, PKF050-638, CBS9106, and Selinexor. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is Leptomycin B. In some ~~embodiment~~examples, the nucleocytoplasmic transport inhibitor is Selinexor. In some ~~embodiment~~examples, the cell is a Human A549 cell, a HeLa cell, a 239 cell, or a primate Vero cell. In some ~~embodiment~~examples, the cell is a human cell. In some ~~embodiment~~examples, the cell is an in vivo cell, an in vitro cell, or an ex vivo cell. In some ~~embodiment~~examples, the cancer is a solid tumor. In some ~~embodiment~~examples, the solid tumor is a sarcoma or a carcinoma. In some ~~embodiment~~examples, the solid tumor is fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, uterine cancer, testicular cancer, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma,

hemangioblastoma, acoustic neuroma, oligodendroglioma, schwannoma, meningioma, melanoma, neuroblastoma, or retinoblastoma. In some ~~embodiment~~examples, the solid tumor is colorectal adenocarcinoma, pancreatic cancer, or melanoma. In some ~~embodiment~~examples, the oncolytic virus and said nucleocytoplasmic transport inhibitor are administered simultaneously or sequentially. In some ~~embodiment~~examples, the oncolytic virus is administered before administering said nucleocytoplasmic transport inhibitor. In some ~~embodiment~~examples, the oncolytic virus is administered after administering said nucleocytoplasmic transport inhibitor. In some ~~embodiment~~examples, the method comprises administering said oncolytic virus and said nucleocytoplasmic transport inhibitor for a period of at least 1 day, at least 2 days, at least 3 days, at least 1 week, at least 2 weeks, at least 3 weeks, at least 4 weeks, at least 1 month, at least 3 months, at least 6 months, or at least 1 year. In some ~~embodiment~~examples, the method comprises administering said oncolytic virus, said nucleocytoplasmic transport inhibitor, or both to said subject twice a week, once a week, once every two weeks, once every three weeks, once every four weeks, once a month, or once every two months. In some ~~embodiment~~examples, the oncolytic virus is administered locally to a cancer tissue to be treated. In some ~~embodiment~~examples, the oncolytic virus is administered by injection. In some ~~embodiment~~examples, a multiplicity of infection (MOI) of said oncolytic virus for said tissue is from about 0.01 to about 10. In some ~~embodiment~~examples, a multiplicity of infection (MOI) of said oncolytic virus for said tissue is from about 0.05 to about 5. In some ~~embodiment~~examples, a concentration of said nucleocytoplasmic transport inhibitor at said tissue is from about 0.0001 μM to about 100 μM. In some ~~embodiment~~examples, a concentration of said nucleocytoplasmic transport inhibitor at said tissue is from about 0.01 μM to about 1 μM. In some ~~embodiment~~examples, the method comprises contacting said cancer cell with said oncolytic virus and said nucleocytoplasmic transport inhibitor simultaneously or sequentially. In some ~~embodiment~~examples, the cancer cell is contacted with said oncolytic virus before with said nucleocytoplasmic transport inhibitor. In some ~~embodiment~~examples, the cancer cell is contacted with said nucleocytoplasmic transport inhibitor before with said oncolytic virus. In some ~~embodiment~~examples, the method comprises pre-treating said cancer cell with said nucleocytoplasmic transport inhibitor before said cancer cell is contacted with said oncolytic virus. In some ~~embodiment~~examples, the cancer cell is contacted with said oncolytic virus at an MOI of from about 0.01 to about 10. In some ~~embodiment~~examples, the cancer cell is contacted with said oncolytic virus at an MOI of from about 0.05 to about 5. In some ~~embodiment~~examples, the method comprises incubating said cancer cell in a media comprising said nucleocytoplasmic transport inhibitor at a concentration of from about 0.0001 μM to about 100 μM. In some ~~embodiment~~examples, the method comprises incubating said cancer cell in a media comprising said nucleocytoplasmic transport inhibitor at a concentration of from about 0.01 μM to about 1 μM. In some ~~embodiment~~examples, the method comprises contacting said cancer cell with a media comprising said nucleocytoplasmic

transport inhibitor at a concentration of from about 0.0001 μM to about 100 μM. In some ~~embodiment~~examples, the method comprises contacting said cancer cell with a media comprising said nucleocytoplasmic transport inhibitor at a concentration of from about 0.01 μM to about 1 μM. In some ~~embodiment~~examples, the method comprises contacting said oncolytic virus to an autologous or heterologous cell *ex vivo*. In some ~~embodiment~~examples, the autologous or heterologous cell is a bone marrow cell or a macrophage cell. In some ~~embodiment~~examples, the method comprises injecting said autologous or heterologous cell into said subject.

[0017] In one ~~aspect~~example, described herein is a pharmaceutical composition comprising: an oncolytic virus, and a nucleocytoplasmic transport inhibitor. In some ~~embodiment~~examples, the pharmaceutical composition further comprises a pharmaceutically acceptable excipient or carrier. In some ~~embodiment~~examples, the pharmaceutical composition is in a unit dosage form suitable for intratumorally or parenterally administration. In some ~~embodiment~~examples, the unit dosage comprises from about $1x10^3$ plaque-forming units (PFU) to about $1x10^{10}$ PFU of the oncolytic virus per mL. In some ~~embodiment~~examples, the unit dosage comprises from about $1x10^5$ PFU to about $1x10^{10}$ PFU of the oncolytic virus per mL. In some ~~embodiment~~examples, a weight ratio between said oncolytic virus and said nucleocytoplasmic transport inhibitor is from about $1x10^9$ to about $1x10^{-9}$.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] **FIG. 1A** and **FIG. 1B** illustrates the treatment of human colorectal adenocarcinoma cell line HT29 with nucleocytoplasmic transport inhibitor Leptomycin B enhanced MYXV early (GFP) and late (TdTomato) gene expression levels. HT29 cells were pre-treated with different concentrations of Leptomycin B for 1h and infected with vMyx-GFP-Tdtomato at an MOI of 5.0 (**FIG.1A**) or 0.5 (**FIG. 1B**) in the presence of the inhibitor, and fluorescence images were taken at 24h (**FIG. 1A**) and 48h (**FIG. 1B**) post infection (HPI) using a fluorescence microscope.

[0019] **FIG. 2** illustrates that nucleocytoplasmic transport inhibitor Leptomycin B enhanced MYXV replication in human colorectal adenocarcinoma cell line HT29. HT29 cells were pre-treated with different concentration of Leptomycin B for 1h. The cells were then infected with vMyx-GFP-TdTomato at an MOI of 0.5 or 0.05 for 1h. After 1h the un-adsorbed viruses were removed, the cells were washed and incubated with media in the presence of the inhibitor. The infected cells were harvested after 72h post infection and virus titers were determined following serial dilutions onto RK13 cells.

CLAIMS

We Claim:

1. Use of~~A method of treating cancer, comprising administering to a subject~~ a therapeutically effective amount of an oncolytic virus in the manufacture of a first medicament, and a nucleocytoplasmic transport inhibitor in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating cancer, wherein the first and second medicaments are to be administered to a subject.
2. The use~~method~~ of claim 1, wherein the oncolytic virus is derived~~-~~ from the *Poxviridae* family.
3. The use~~method~~ of any one of claims 1 or 2, wherein the oncolytic virus is derived from *Chordopoxvirinae* subfamily or *Entomopoxvirinae* subfamily.
4. The use~~method~~ of any one of claims 1 to 3, wherein the oncolytic virus is derived from a virus genus of *Orthopoxvirus*, *Cervidpoxvirus*, *Parapoxvirus*, *Avipoxvirus*, *Capripoxvirus*, *Leporipoxvirus*, *Suipoxvirus*, *Molluscipoxvirus*, *Yatapoxvirus*, *Alphaentomopoxvirus*, *Betaentomopoxvirus*, or *Gammaentopoxvirus*.
5. The use~~method~~ of any one of claims 1 to 4, wherein the oncolytic virus is derived from genus *Leporipoxvirus*.
6. The use~~method~~ of any one of claims 1 to 5, wherein the oncolytic virus is a *myxoma virus* (MYXV).
7. The use~~method~~ of any one of claims 1 to 4, wherein the oncolytic virus is derived from genus *Orthopoxvirus*.
8. The use~~method~~ of any one of claims 1 to 7, wherein the virus is genetically modified.
9. The use~~method~~ of any one of claims 1 to 8, wherein the nucleocytoplasmic transport inhibitor is selected from the group consisting of Leptomycin A, Leptomycin B, Ratjadone A, Ratjadone B, Ratjadone C, Ratjadone D, Anguinomycin A, Goniothalamin, piperlongumine, plumbagin, curcumin, valtrate, acetoxychavicol acetate, prenylcoumarin osthol, KOS 2464, PKF050-638, CBS9106, and Selinexor.
10. The use~~method~~ of any one of claims 1 to 9, wherein the nucleocytoplasmic transport inhibitor is Leptomycin B.
11. The use~~method~~ of any one of claims 1 to 9, wherein the nucleocytoplasmic transport inhibitor is Selinexor.
12. The use~~method~~ of any one of claims 1 to 11, wherein the cancer is a solid tumor.
13. The use~~method~~ of claim 12, wherein the solid tumor is a sarcoma or a carcinoma.

14. The use~~method~~ of claim 12, wherein the solid tumor is fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical cancer, uterine cancer, testicular cancer, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, schwannoma, meningioma, melanoma, neuroblastoma, or retinoblastoma.
15. The use~~method~~ of claim 12, wherein the solid tumor is colorectal adenocarcinoma, pancreatic cancer, or melanoma.
16. The use~~method~~ of any one of claims 1 to 15, wherein the oncolytic virus and the nucleocytoplasmic transport inhibitor are to be administered simultaneously.
17. The use~~method~~ of any one of claims 1 to 15, wherein the oncolytic virus and the nucleocytoplasmic transport inhibitor are to be administered sequentially
18. The use~~method~~ of clam 17, wherein the oncolytic virus is to be administered before ~~administering~~ the nucleocytoplasmic transport inhibitor is to be administered.
19. The use~~method~~ of claim 17, wherein the oncolytic virus is to be administered after ~~administering~~ the nucleocytoplasmic transport inhibitor is to be administered.
20. The use~~method~~ of any one of claims 1 to 19, wherein ~~the method comprises administering~~ the oncolytic virus and the nucleocytoplasmic transport inhibitor are to be administered for a period of at least 1 day, at least 2 days, at least 3 days, at least 1 week, at least 2 weeks, at least 3 weeks, at least 4 weeks, at least 1 month, at least 3 months, at least 6 months, or at least 1 year.

~~21. The method of any one of claims 1 to 20, wherein the method comprises administering the oncolytic virus, the nucleocytoplasmic transport inhibitor, or both to the subject twice a week, once a week, once every two weeks, once every three weeks, once every four weeks, once a month, or once every two months.~~

~~22. The method of any one of claims 1 to 21, wherein the oncolytic virus is administered locally to a cancer tissue to be treated.~~

~~23. The method of claim 22, wherein the oncolytic virus is administered by intratumoral injection.~~

~~24. The method of claim 22 or 23, wherein a multiplicity of infection (MOI) of the oncolytic virus for the tissue is from about 0.01 to about 10.~~

~~25. The method of any one of claims 22-24, wherein a multiplicity of infection (MOI) of the oncolytic virus for the tissue is from about 0.05 to about 5.~~

~~26. The method of any one of claims 22-25, wherein a concentration of the nucleocytoplasmic transport inhibitor at the tissue is from about 0.0001 μM to about 100 μM.~~

~~27. The method of any one of claims 22-26, wherein a concentration of the nucleocytoplasmic transport inhibitor at the tissue is from about 0.01 μM to about 1 μM.~~

~~28. A method of killing a cancer cell comprising: contacting the cancer cell with an oncolytic virus and a nucleocytoplasmic transport inhibitor, thereby killing the cancer cell.~~

~~29. A method of enhancing susceptibility of a cancer cell to infection by an oncolytic virus, comprising contacting the cancer cell to an oncolytic virus and a nucleocytoplasmic transport inhibitor.~~

~~30. A method of inducing a cancer cell to be susceptible to infection by an oncolytic virus, comprising contacting the cancer cell to the oncolytic virus and a nucleocytoplasmic transport inhibitor.~~

~~31. A method of converting a nonpermissive cancer cell to a permissive cancer cell comprising contacting the nonpermissive cancer cell with an oncolytic virus and a nucleocytoplasmic transport inhibitor.~~

~~32. A method of increasing proliferation of an oncolytic virus in a cancer cell that is not susceptible to infection by the oncolytic virus comprising contacting the cancer cell to an oncolytic virus and a nucleocytoplasmic transport inhibitor.~~

~~33. The method of any one of claims 28-32, wherein said oncolytic virus is a virus from the *Poxviridae* family.~~

~~34. The method of any one of claims 28-33, wherein said oncolytic virus is a virus from *Chordopoxvirinae* subfamily or *Entomopoxvirinae* subfamily.~~

~~35. The method of any one of claims 28-34, wherein said oncolytic virus is from a virus genus that is *Orthopoxvirus*, *Cervidpoxvirus*, *Parapoxvirus*, *Avipoxvirus*, *Capripoxvirus*, *Leporipoxvirus*, *Suipoxvirus*, *Molluscipoxvirus*, *Yatapoxvirus*, *Alphaentomopoxvirus*, *Betaentomopoxvirus*, or *Gammaentopoxvirus*.~~

~~36. The method of any one of claims 28-35, wherein said oncolytic virus is from genus *Leporipoxvirus*.~~

37. The method of any one of claims 28-36, wherein said oncolytic virus is a *myxoma virus* (MYXV).

38. The method of any one of claims 28-35, wherein said oncolytic virus is from genus *Orthopoxvirus*.

39. The method of any one of claims 28-36, wherein said virus is genetically modified.

40. The method of any one of claims 28-39, wherein said nucleocytoplasmic transport inhibitor is selected from the group consisting of Leptomycin A, Leptomycin B, Ratjadone A, Ratjadone B, Ratjadone C, Ratjadone D, Anguinomycin A, Goniothalamin, piperlongumine, plumbagin, curcumin, valtrate, acetoxychavicol acetate, prenylcoumarin osthol, KOS-2464, PKF050-638, CBS9106, and Selinexor.

41. The method of any one of claims 28-40, wherein said nucleocytoplasmic transport inhibitor is Leptomycin B.

42. The method of any one of claims 28-40, wherein said nucleocytoplasmic transport inhibitor is Selinexor.

43. The method of any one of claims 28-42, wherein the cancer cell is colorectal cancer cell, pancreatic cancer cell, melanoma cancer cell.

44. The method of any one of claims 28-43, wherein the cancer cell is a human cancer cell.

45. The method of any one of claims 28-44, wherein the cancer cell is contacted to an oncolytic virus and a nucleocytoplasmic transport inhibitor *in vivo*.

46. The method of any one of claims 28-44, wherein the cancer cell is contacted to an oncolytic virus and a nucleocytoplasmic transport inhibitor *ex vivo*.

47. The method of any one of claims 28-46, wherein the method comprises contacting the cancer cell with the oncolytic virus and the nucleocytoplasmic transport inhibitor simultaneously.

48. The method of any one of claims 28-46, wherein the method comprises contacting the cancer cell with the oncolytic virus and the nucleocytoplasmic transport inhibitor sequentially.

49. The method of claim 48, wherein the cancer cell is contacted with the oncolytic virus before being contacted with the nucleocytoplasmic transport inhibitor.

50. The method of claim 48, wherein the cancer cell is contacted with the nucleocytoplasmic transport inhibitor before being contacted with the oncolytic virus.

51. The method of any one of claims 28-50, wherein the cancer cell is contacted with the oncolytic virus at a MOI of from about 0.01 to about 10.

52. The method of any one of claims 28-51, wherein the cancer cell is contacted with the oncolytic virus at a MOI of from about 0.05 to about 5.

53. The method of any one of claims 28-52, wherein the method comprises incubating the cancer cell in a media comprising the nucleocytoplasmic transport inhibitor at a concentration of from about 0.0001 μM to about 100 μM.

54. The method of any one of claims 28-53, wherein the method comprises incubating the cancer cell in a media comprising the nucleocytoplasmic transport inhibitor at a concentration of from about 0.01 μM to about 1 μM.

55. The method of any one of claims 28-54, wherein the method comprises contacting the cancer cell with a media comprising the nucleocytoplasmic transport inhibitor at a concentration of from about 0.0001 μM to about 100 μM.

56. The method of any one of claims 28-55, wherein the method comprises contacting the cancer cell with a media comprising the nucleocytoplasmic transport inhibitor at a concentration of from about 0.01 μM to about 1 μM.

57. The method of any one of claims 28-56, further comprising contacting the oncolytic virus to an autologous or heterologous cell *ex vivo*.

58. The method of claim 57, wherein the autologous or heterologous cell is a bone marrow cell or a macrophage cell.

59. The method of claim 57-58, further comprising injecting the autologous or heterologous cell to the subject.

60. A pharmaceutical composition comprising:

a. an oncolytic virus, and

b. a nucleocytoplasmic transport inhibitor.

61. The pharmaceutical composition of claim 60, further comprising a pharmaceutically acceptable excipient or carrier.

62. The pharmaceutical composition of any one of claims 60-61, wherein the oncolytic virus is derived from the *Poxviridae* family.

63. The pharmaceutical composition of any one of claims 60-62, wherein the oncolytic virus is derived from *Chordopoxvirinae* subfamily or *Entomopoxvirinae* subfamily.

64. The pharmaceutical composition of any one of claims 60-63, wherein the oncolytic virus is derived from a virus genus of *Orthopoxvirus*, *Cervidpoxvirus*, *Parapoxvirus*, *Avipoxvirus*, *Capripoxvirus*, *Leporipoxvirus*, *Suipoxvirus*, *Molluscipoxvirus*, *Yatapoxvirus*, *Alphaentomopoxvirus*, *Betaentomopoxvirus*, or *Gammaentopoxvirus*.

65. The pharmaceutical composition of any one of claims 60-64, wherein the oncolytic virus is derived from genus *Leporipoxvirus*.

66. The pharmaceutical composition of any one of claims 60-65, wherein the oncolytic virus is a *myxoma virus* (MYXV).

67. The pharmaceutical composition of any one of claims 60-64, wherein the oncolytic virus is derived from genus *Orthopoxvirus*.

68. The pharmaceutical composition of any one of claims 60-67, wherein the virus is genetically modified.

69. The pharmaceutical composition of any one of claims 60-68, wherein the nucleocytoplasmic transport inhibitor is selected from the group consisting of Leptomycin A, Leptomycin B, Ratjadone A, Ratjadone B, Ratjadone C, Ratjadone D, Anguinomycin A, Goniothalamin, piperlongumine, plumbagin, curcumin, valtrate, acetoxychavicol acetate, prenylcoumarin osthol, KOS 2464, PKF050-638, CBS9106, and Selinexor.

70. The pharmaceutical composition of any one of claims 60-69, wherein the nucleocytoplasmic transport inhibitor is Leptomycin B.

71. The pharmaceutical composition of any one of claims 60-70, wherein the nucleocytoplasmic transport inhibitor is Selinexor.

72. The pharmaceutical composition of any one of claims 60-71, wherein the pharmaceutical composition is in a unit dosage form suitable for intratumoral or parenteral administration.

73. The pharmaceutical composition of claim 72, wherein the unit dosage comprises from about $1x10^3$ plaque-forming units (PFU) to about $1x10^{10}$ PFU of the oncolytic virus per mL.

74. The pharmaceutical composition of claim 72, wherein the unit dosage comprises from about $1x10^5$ PFU to about $1x10^{10}$ PFU of the oncolytic virus per mL.

75. The pharmaceutical composition of any one of claims 60-74, wherein a weight ratio between the oncolytic virus and the nucleocytoplasmic transport inhibitor is from about $1x10^9$ to about $1x10^{-9}$.