(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 October 2020 (15.10.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/210711 A1

(51) International Patent Classification:
A61K 35/76 (2015.01) *A61P 31/12* (2006.01)
A61K 35/768 (2015.01) *A61P 35/00* (2006.01)
A61K 38/21 (2006.01) *C12N 7/00* (2006.01)

(21) International Application Number:
PCT/US2020/027784

(22) International Filing Date:
10 April 2020 (10.04.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/832,509 11 April 2019 (11.04.2019) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,

(54) Title: COMPOSITIONS AND METHODS OF USING SENECA VALLEY VIRUS (SVV) FOR TREATING CANCER

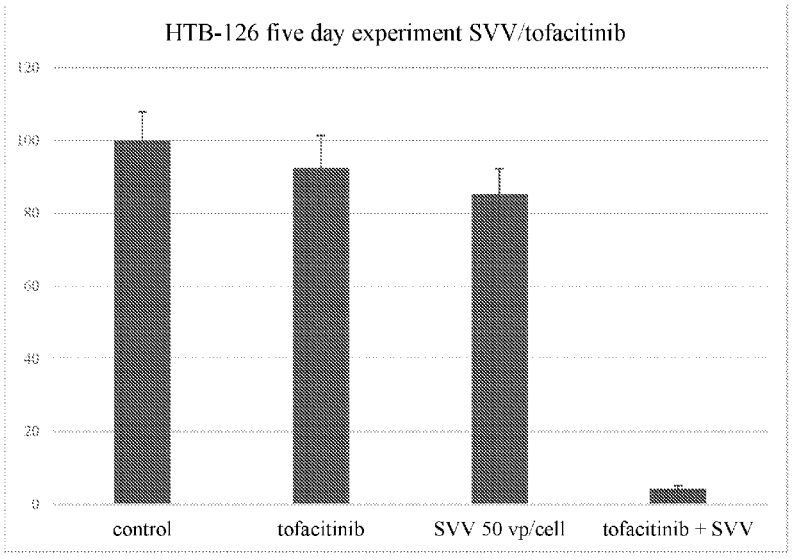


Figure 1

(57) Abstract: Provided herein are compositions and methods of using Seneca Valley Virus (SW),or a derivative thereof, combined with an IFN-I inhibitor for treating a cancer in a subject. The disclosed methods particularly rely upon the expression level of an ANTXR1 and the expression level of IFN-I in the cancer from the subject. Also provided herein are methods for predicting the efficacy of an SW treatment and a kit for determining the same.

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TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

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COMPOSITIONS AND METHODS OF USING SENECA VALLEY VIRUS (SVV) FOR TREATING CANCER

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. provisional application number 62/832,509, filed April 11, 2019, the disclosure of which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] The disclosed inventions relate to compositions and methods for treating cancer. More particularly, the disclosed inventions relate to the field of treating cancer in a subject using an oncolytic virus.

BACKGROUND

[0003] Oncolytic viruses have shown great potential as anti-cancer agents thanks to their ability kill tumors in the absence of damage to normal cells. The oncolytic virus Seneca Valley Virus (SVV) was originally shown to replicate and kill cancer cells with neuroendocrine properties, such as small cell lung cancer (SCLC), a variety of solid pediatric cancers, and carcinoid cancers. Unfortunately, both SCLC and solid pediatric cancer patients are some of the most difficult cancers to treat because of the short life span of patients following their failure to respond to standard of care therapy or have developed resistance. Data from clinical trials showed no evidence of SVV infection or replication within normal tissue surrounding the tumor. However, despite great potential for SVV based oncolytic viral therapies many tumors did not respond to SVV therapy.

[0004] Anthrax toxin receptor 1 (ANTXR1) is known to promote angiogenesis during disease development and is not required for normal cellular physiology. Recently, ANTXR1 was shown to interact directly and specifically with SVV. ANTXR1 expression on tumor cells was proven to be essential for SVV infection. However, the presence of ANTXR1 on various type of solid cancer tumors is not sufficient to favor an optimal permissivity and replication of SVV and thus killing of cancer cells.

SUMMARY

[0005] Provided herein are methods of treating a cancer in a subject in need thereof. The methods comprise administering to the subject an effective amount of Seneca Valley Virus (SVV) or SVV derivative, wherein the cancer is characterized by (a) an expression level of anthrax toxin receptor 1 (ANTXRl) higher than an ANTXRl reference value, and (b) an expression level of interferon type I (IFN-I) lower than an IFN-I reference value, wherein the subject is also administered at least one IFN-I inhibiting comprising a JAK inhibitor.

[0006] Also provided herein are other methods of treating a cancer in a subject in need thereof. The methods comprise administering to the subject an IFN-I inhibiting agent comprising a JAK inhibitor and an effective amount of SVV or SVV derivative, wherein the cancer is characterized by an expression level of ANTXRl higher than an ANTXRl reference value, and wherein the IFN-I inhibiting agent reduces the expression level of IFN-I in the cancer thereby favoring replication of the SVV or the SVV derivative and killing of the cancer.

[0007] Also provided herein are methods of predicting the efficacy of a cancer treatment comprising an Seneca Valley Virus (SVV), or an SVV derivative, combined with at least one IFN-I inhibiting agent comprising a JAK inhibitor. The methods comprise determining the expression level of ANTXRl and the expression level of IFN-I in the cancer from a subject, wherein (a) an expression level of ANTXRl higher than an ANTXRl reference value, and (a) an expression level of IFN-I lower than an IFN-I reference value are predictive that the treatment is effective, and wherein when the treatment is predicted to be effective, recommending treatment of the subject.

[0008] Further provided herein are pharmaceutical compositions for treating a cancer in a subject. The pharmaceutical compositions comprise an IFN-I inhibiting agent comprising a JAK inhibitor, an SVV or an SVV derivative and a pharmaceutical acceptable carrier.

[0009] Also provided are Seneca Valley Virus (SVV) or SVV derivatives in combination with at least one IFN-I inhibiting agent comprising a JAK inhibitor for use in the manufacture of a medicament for treatment of a cancer, wherein the cancer is characterized by an expression level of anthrax toxin receptor 1 (ANTXRl) higher than an ANTXRl reference value, and an expression level of interferon type I (IFN-I) lower than an IFN-I reference value.

[0010] Further provided herein are kits for determining a predisposition of an efficacious response to a cancer treatment comprising an Seneca Valley Virus (SVV), or an SVV

derivative, combined with at least one IFN-I inhibiting agent comprising a JAK inhibitor. The kits comprise a reagent for determining the expression level of ANTXRl and a reagent for determining the expression level of IFN-I in the cancer from a subject.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] For the purpose of illustrating the invention, there are depicted in the drawings certain embodiments of the invention. However, the invention is not limited to the precise arrangements and instrumentalities of the embodiments depicted in the drawings.

[0012] Figure 1 is a histogram depicting an example of the use of a drug to modify susceptibility to virus mediated killing by Seneca Valley Virus (SVV). HTB-126 cells (triple negative breast cancer, TNBC) were pretreated for 24hours in 12.5 micromolar tofacitinib then infected with 50 viral particles (VP) of SVV/cell. Standard deviations of replicates are presented as error bars (VP/cell with 1 PFU or TCID50 unit per 100 VPs).

[0013] Figure 2 is a histogram depicting an example of triple negative breast cancer cells (BT-549) that are susceptible to infection by Seneca Valley Virus. Treatment with various drug compounds showed a substantial enhancement of SVV replication in TNBC cell lines and cell death.

[0014] Figure 3 is a histogram depicting an example of the use of a drug to modify susceptibility to virus mediated killing by Seneca Valley Virus (SVV). U2OS cells (osteosarcoma) were pretreated for 24hours in pharmaceutical compounds to disrupt innate antiviral responses to allow increased viral mediated killing. Ruxolitinib, tofacitinib, and dimethyl fumarate increased Seneca Valley Virus mediated cell killing.

[0015] Figure 4 is a histogram depicting an example of the use of a drug to modify susceptibility to virus mediated killing by Seneca Valley Virus (SVV). HCT-116 cells (Colorectal cancer cells) were pretreated for 24hours in pharmaceutical compounds to disrupt innate antiviral responses to allow increased viral mediated killing. Panobinostat and vorinostat increased Seneca Valley Virus mediated cell killing with a smaller effect shown by tofacitnib and dimethyl fumarate.

[0016] Figure 5 is a histogram showing that the combination SVV and JAKi synergistically kills Triple Negative Breast Cancer (TNBC) lines. SVV is extremely selective toward killing only tumor cells even with inhibiting Type I IFN as the receptor ANTXR1/TEM 8

is extremely selective toward tumor cells. Treatment with Tofacintinib compound (1PFU/cell of SVV and 0.8uM of Tofacintinib) showed a substantial enhancement of SVV replication in TNBC cell lines and cell death.

[0017] Figure 6 is a plot representing a receiver operating characteristic curve (ROC) for an elastic net minimization of predictive genes set (IFN, Myc and IFI35). In order to identify a minimal predictive gene set, an elastic net was used. Area under the curve (AUC) of the receiver operating characteristic was calculated across a range of tuning parameters, lambda, which controls the overall strength of the elastic net penalty. Mean AUC was calculated using 6-fold cross validation (reads points). Uncertainty is expressed as standard deviation. Vertical dashed lines indicate the optimal values of lambda that give either the minimum mean cross-validation error or the model exhibiting error within one standard error of the minimum.

[0018] Figure 7 is a plot representing a ROC showing that a minimal IFN signature performs as well as a complete IFN gene set (with 44 genes).

[0019] Figure 8 is a plot representing a ROC showing that a minimal IFN signature (e.g. IFI35) performs as well as a complete IFN gene set. Receiver operating characteristic curves of minimal interferon signature or the complete IFN gene set were plotted. It was shown that a minimal IFN gene set performed similarly as the full IFN gene set based on Delong's method for comparison of two ROC curves. Sensitivity and specificity were optimal for IFN+ ANTXR1 and minimal IFN + ANTXR1 as compared to ANTXR1 by itself.

[0020] Figure 9 is a heatmap representing the IFN expression matrix for various IFN signature genes in various tumor samples (autonomic ganglia, bone, breast, central, haematopoietic, kidney, large intestine, liver, lung, oesophagus, ovary, pancreas, prostate, skin, soft tissue).

[0021] Figure 10 is a heatmap representing the IFN correlation matrix for various IFN signature genes in various tumor samples (autonomic, bone, breast, central, haematopoietic, kidney, large intestine, liver, lung, oesophagus, ovary, pancreas, prostate, skin, soft tissue).

[0022] Figure 11 is a bar graph illustrating the fractions of tumors (by Site: autonomic ganglia) that are predicted to be only permissive (P) versus non-permissive (NP).

[0023] Figure 12 is a bar graph showing that at least 65% of all solid cancer indications have ANTXR1/TEM 8 expressed a level necessary for SVV infection. 60-95% of major indications express TEM 8. 100% of all solid cancer indications have TEM 8 expressed at high

levels in cancer stromal cells. P: Permissive; NP: Non-Permissive; and HDCAi/JAKi: Permissive upon treatment with HDCA and/or JAK inhibitors.

[0024] Figure 13 is a bar graph illustrating the fractions of lung tumors that are predicted to be permissive. P: Permissive; NP: Non-Permissive; and HDCAi/JAKi: Permissive upon treatment with HDCA and/or JAK inhibitors.

[0025] Figure 14 is a bar graph illustrating the fractions of breast tumors that are predicted to be permissive. P: Permissive; NP: Non-Permissive; and HDCAi/JAKi: Permissive upon treatment with HDCA and/or JAK inhibitors.

[0026] Figure 15 is a bar graph illustrating the fractions of bone tumors that are predicted to be permissive. P: Permissive; NP: Non-Permissive; and HDCAi/JAKi: Permissive upon treatment with HDCA and/or JAK inhibitors.

[0027] Figure 16 is a bar plot illustrating the fractions of breast tumors that are predicted to be permissive (by driver). P: Permissive; NP: Non-Permissive; and HDCAi/JAKi: Permissive upon treatment with HDCA and/or JAK inhibitors.

[0028] Figure 17 is a graph illustrating the fractions of breast tumors that are predicted to be permissive (by driver). P: Permissive; NP: Non-Permissive; and HDCAi/JAKi: Permissive upon treatment with HDCA and/or JAK inhibitors.

[0029] Figure 18 is a graph representing the AUC minimization with a 0.9 cut off value for the predictive analysis.

[0030] Figure 19 is a table listing series of data predictions for cancer cell lines and their predicted status for permissive or non-permissive SVV replication.

DETAILED DESCRIPTION OF THE INVENTION

[0031] The present invention relates to compositions and methods of using Seneca Valley Virus (SVV) or a derivative thereof for treating cancer in a subject. The SVV and SVV derivatives of the invention are useful in a variety of applications such as treating a cancer, reducing or inhibiting cancer cells growth, and increasing the survival of subject suffering from cancer. The disclosed methods particularly rely upon the level of an ANTXRl expression and the level of IFN-I expression in a cancerous tissue from the subject. Also provided herein are methods for predicting the efficacy of an SVV treatment and a kit for determining the same.

Definitions

[0032] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention pertains. Although any methods and materials similar or equivalent to those described herein may be used in the practice for testing of the present invention, the preferred materials and methods are described herein. In describing and claiming the present invention, the following terminology will be used.

[0033] It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting.

[0034] As used herein, the articles "a" and "an" are used to refer to one or to more than one (*i.e.*, to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

[0035] As used herein the terms anthrax toxin receptor 1 (ANTXR1) or Tumor Endothelial Marker 8 (TEM8), are used interchangeably. The protein encoded by ANTXR1 gene is a type I transmembrane protein. ANTXR1/TEM8 is a tumor-specific endothelial marker that has been implicated tumor vasculature formation of various cancers (e.g. colorectal).

[0036] As used herein when referring to a measurable value such as an amount, a temporal duration, and the like, the term "about" is meant to encompass variations of ±20% or ±10%, more preferably ±5%, even more preferably ±1%, and still more preferably ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

[0037] The term "biological" or "biological sample" refers to a sample obtained from an organism or from components (e.g., cells) of an organism. The sample may be of any biological tissue or fluid. Frequently the sample will be a "clinical sample" which is a sample derived from a patient. Such samples include, but are not limited to, bone marrow, cardiac tissue, sputum, blood, lymphatic fluid, blood cells (e.g., white cells), tissue or fine needle biopsy samples, urine, peritoneal fluid, and pleural fluid, or cells therefrom. Biological samples may also include sections of tissues such as frozen sections taken for histological purposes.

[0024] As used herein, the terms "comprising," "including," "containing" and "characterized by" are exchangeable, inclusive, open-ended and do not exclude additional, unrecited elements or method steps. Any recitation herein of the term "comprising," particularly in a description of components of a composition or in a description of elements of a device, is

understood to encompass those compositions and methods consisting essentially of and consisting of the recited components or elements.

[0025] As used herein, the term "consisting of" excludes any element, step, or ingredient not specified in the claim element.

[0038] As used herein, the terms "derivative" specifies that a derivative of a virus can have a nucleic acid or amino acid sequence difference in respect to a template viral nucleic acid or amino acid sequence. For instance, an SVV derivative can refer to an SVV that has a nucleic acid or amino acid sequence different with respect to the wild-type SVV nucleic acid or amino acid sequence of ATCC Patent Deposit Number PTA-5343. In some embodiments, the SVV derivative encompasses an SVV mutant, an SVV variant or a modified SVV (e.g. genetically engineered SVV). In some embodiments, the modify SVV derivative is modified to be capable of recognizing different cell receptors or to be capable of evading the immune system while still being able to invade, replicate and kill the cell of interest (i.e. cancer cell). In general, an SVV or SVV derivative can be derived from an already pre-existing stock of virus that is passaged to produce more viruses. SVV or SVV derivative can also be derived from a plasmid.

[0039] As used herein, "higher" refers to expression levels which are at least 10% or more, for example, 20%, 30%, 40%, or 50%, 60%, 70%, 80%, 90% higher or more, and/or 1.1 fold, 1.2 fold, 1.4 fold, 1.6 fold, 1.8 fold, 2.0 fold higher or more, and any and all whole or partial increments therebetween, than a control reference. A disclosed herein an expression level higher than a reference value refers to an expression level (mRNA or protein) that is higher than a normal or control level from an expression (mRNA or protein) measured in a healthy subject or defined or used in the art.

[0040] As used herein, "lower" refers to expression levels which are at least 10% lower or more, for example, 20%, 30%, 40%, or 50%, 60%, 70%, 80%, 90% lower or more, and/or 1.1 fold, 1.2 fold, 1.4 fold, 1.6 fold, 1.8 fold, 2.0 fold lower or more, and any and all whole or partial increments in between, than a control reference. A disclosed herein an expression level lower than a reference value refers to an expression level (mRNA or protein) that is lower than a normal or control level from an expression (mRNA or protein) measured in a healthy subject or defined or used in the art.

[0041] As used herein, the terms "control," or "reference" can be used interchangeably and refer to a value that is used as a standard of comparison.

[0042] As used herein, by "combination therapy" is meant that a first agent is administered in conjunction with another agent. "In combination with" or "In conjunction with" refers to administration of one treatment modality in addition to another treatment modality. As such, "in combination with" refers to administration of one treatment modality before, during, or after delivery of the other treatment modality to the individual. Such combinations are considered to be part of a single treatment regimen or regime.

[0043] The term "Type I interferon (IFN-I)" refers herein to interferon proteins or genes involved in regulating the activity of the immune system with antiviral, antitumor and immunoregulatory functions. As used herein, IFN-I includes any set of proteins, genes or transcripts that comprise or regulate the type I IFN pathway. Examples of IFN-I in mammals include but are not limited to IFN-α (alpha), IFN-β (beta), IFN-κ (kappa), IFN-δ (delta), IFN-ε (epsilon), IFN-τ (tau), IFN-ω (omega), and IFN-ζ (zeta). IFN-I biomarkers (mRNA or protein) may include various cytokines (interferons, interleukins or other growth factors). For instance, IFN-I biomarkers can comprise IFI35, IFN-α, IFN-β, IFN-κ, IFN-δ, IFN-ε, IFN-τ, IFN-ω, and IFN-ζ, ADAR, IRF9, IFITM3, IFITM2, USP18, LOC144383, EGR1, IFI6, GBP2, HLA-A, HLA-B, HLA-C, HLA-F, HLA-G, IRF8, IFI27, IFI35, IFIT2, IFIT1, IFIT3, IFNA1, IFNA2, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNA10, IFNA14, IFNA16, IFNA17, IFNA21, IFNAR1, IFNAR2, IFNB1, IRF1, IRF2, IRF3, IRF4, IRF5, IRF6, IRF7, ISG20, JAK1, MX1, MX2, OAS1, OAS2, OAS3, IP6K2, XAF1, PSMB8, PTPN1, PTPN6, RNASEL, HLA-K, STAT1, STAT2, TYK2, HLA-B, IFITM1, OASL, SOCS1, SOCS3 and ISG15.

[0044] As used herein, the terms "peptide," "polypeptide," and "protein" are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed on the maximum number of amino acids that may comprise a protein or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. The

polypeptides include natural peptides, recombinant peptides, synthetic peptides, or a combination thereof.

[0045] As used herein, plaque forming units (PFU) refers to a measure of number of infectious virus particles. It is determined by plaque forming assay.

[0046] As used herein, multiplicity of infection (MOI) refers the average number of virus particles infecting each cell. MOI can be related to PFU by the following formula:

[0047] Multiplicity of infection (MOI) = Plaque forming units (PFU) of virus used for infection / number of cells.

[0048] The term "RNA" as used herein is defined as ribonucleic acid.

[0049] The term "treatment" as used within the context of the present invention is meant to include therapeutic treatment as well as prophylactic, or suppressive measures for the disease or disorder. As used herein, the term "treatment" and associated terms such as "treat" and "treating" means the reduction of the progression, severity and/or duration of a disease condition or at least one symptom thereof. The term 'treatment' therefore refers to any regimen that can benefit a subject. The treatment may be in respect of an existing condition or may be prophylactic (preventative treatment). Treatment may include curative, alleviative or prophylactic effects. References herein to "therapeutic" and "prophylactic" treatments are to be considered in their broadest context. The term "therapeutic" does not necessarily imply that a subject is treated until total recovery. Similarly, "prophylactic" does not necessarily mean that the subject will not eventually contract a disease condition. Thus, for example, the term treatment includes the administration of an agent prior to or following the onset of a disease or disorder thereby preventing or removing all signs of the disease or disorder. As another example, administration of the agent after clinical manifestation of the disease to combat the symptoms of the disease comprises "treatment" of the disease.

[0050] As used herein, the term "nucleic acid" refers to polynucleotides such as deoxyribonucleic acid (DNA), and, where appropriate, ribonucleic acid (RNA). The term should also be understood to include, as equivalents, analogs of either RNA or DNA made from nucleotide analogs, and, as applicable to the embodiment being described, single (sense or antisense) and double-stranded polynucleotides. ESTs, chromosomes, cDNAs, mRNAs, and rRNAs are representative examples of molecules that may be referred to as nucleic acids.

[0051] As used herein, the term "pharmaceutical composition" refers to a mixture of at least one compound useful within the invention with other chemical components, such as carriers, stabilizers, diluents, adjuvants, dispersing agents, suspending agents, thickening agents, and/or excipients. The pharmaceutical composition facilitates administration of the compound to an organism. Multiple techniques of administering a compound exist in the art including, but not limited to: intra-tumoral, intravenous, intrapleural, oral, aerosol, parenteral, ophthalmic, pulmonary and topical administration.

[0052] The language "pharmaceutically acceptable carrier" includes a pharmaceutically acceptable salt, pharmaceutically acceptable material, composition or carrier, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material, involved in carrying or transporting a compound(s) of the present invention within or to the subject such that it may perform its intended function. Typically, such compounds are carried or transported from one organ, or portion of the body, to another organ, or portion of the body. Each salt or carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation, and not injurious to the subject. Some examples of materials that may serve as pharmaceutically acceptable carriers include: sugars, such as lactose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol; phosphate buffer solutions; diluent; granulating agent; lubricant; binder; disintegrating agent; wetting agent; emulsifier; coloring agent; release agent; coating agent; sweetening agent; flavoring agent; perfuming agent; preservative; antioxidant; plasticizer; gelling agent; thickener; hardener; setting agent; suspending agent; surfactant; humectant; carrier; stabilizer; and other non-toxic compatible substances employed in pharmaceutical formulations, or any combination thereof. As used herein, "pharmaceutically acceptable carrier" also includes any and all coatings, antibacterial and antifungal agents, and absorption delaying agents, and the like that are

compatible with the activity of the compound, and are physiologically acceptable to the subject. Supplementary active compounds may also be incorporated into the compositions.

[0053] As used herein, the term "effective amount" or "therapeutically effective amount" means the amount of the virus particle or infectious units generated from vector of the invention which is required to prevent the particular disease condition, or which reduces the severity of and/or ameliorates the disease condition or at least one symptom thereof or condition associated therewith.

[0054] A "subject" or "patient," as used therein, may be a human or non-human mammal. Non-human mammals include, for example, livestock and pets, such as ovine, bovine, porcine, canine, feline and murine mammals. Preferably, the subject is a human.

[0055] Ranges: throughout this disclosure, various aspects of the invention can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. This applies regardless of the breadth of the range.

Description

[0056] Provided herein are compositions and methods for treating a cancer in a subject based upon the expression level of an ANTXRl and the expression level of IFN-I expression in the cancer from the subject.

[0057] Methods of the invention

[0058] In one aspect, a method of treating a cancer in a subject in need thereof is disclosed herein. The method comprises administering an effective amount of Seneca Valley Virus (SVV) or SVV derivative, wherein the cancer is characterized by (a) an expression level of anthrax toxin receptor 1 (ANTXRl) higher than an ANTXRl reference value, and (b) an expression level of interferon type I (IFN-I) lower than an IFN-I reference value.

[0059] In one aspect, another method of treating a cancer in a subject in need thereof is disclosed. The method comprises administering to the subject an IFN-I inhibiting agent and an effective amount of SVV or SVV derivative, wherein the cancer is characterized by an expression level of ANTXRl higher than an ANTXRl reference value, and wherein the IFN-I inhibiting agent reduces the expression level of IFN-I in the cancer thereby favoring replication of the SVV or SVV derivative and killing of the cancer.

[0060] In another aspect, also disclosed herein is a method of predicting the efficacy of an SVV or an SVV derivative treatment of a cancer in a subject in need thereof. The method comprises determining the expression level of ANTXRl and the expression level of IFN-I in the cancer from the subject, wherein (a) an expression level of ANTXRl higher than an ANTXRl reference value, and (b) an expression level of IFN-I lower than an IFN-I reference value, are predictive that the treatment is effective, and wherein when the treatment is predicted to be effective, recommending treatment of the subject.

[0061] The treatment of cancer provided herein may include the treatment of solid tumors or the treatment of metastasis. Metastasis is a form of cancer wherein the transformed or malignant cells are traveling and spreading the cancer from one site to another. Such cancers include cancers of the skin, breast, brain, cervix, testes, etc. More particularly, cancers may include, but are not limited to the following organs or systems: cardiac, lung, gastrointestinal, genitourinary tract, liver, bone, nervous system, gynecological, hematologic, skin, and adrenal glands. More particularly, the methods herein can be used for treating gliomas (Schwannoma, glioblastoma, astrocytoma), neuroblastoma, pheochromocytoma, paraganlioma, meningioma, adrenalcortical carcinoma, kidney cancer, vascular cancer of various types, osteoblastic osteocarcinoma, prostate cancer, ovarian cancer, uterine leiomyomas, salivary gland cancer, choroid plexus carcinoma, mammary cancer, pancreatic cancer, colon cancer, and megakaryoblastic leukemia. Skin cancer includes malignant melanoma, basal cell carcinoma, squamous cell carcinoma, Karposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, and psoriasis.

[0062] In some embodiments, the cancer treated by the presently disclosed methods comprises a triple negative breast cancer, a small cell lung cancer, a non-small cell lung cancer, a non-small cell squamous carcinoma, an adenocarcinoma, a glioblastoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial

cancer, a neuroendocrine cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

[0063] Reference value or Control

[0064] The methods provided herein include comparing a measured expression level of ANTXR1 or IFN-I in a cancer from a subject to a reference value (i.e. the control amount) of expression of ANTXR1 or IFN-I.

[0065] In one embodiment, the reference level of expression of ANTXR1 or IFN-I may be obtained by measuring the expression level of ANTXR1 or IFN-I in a healthy subject. Preferably, the healthy subject is a subject of similar age, gender and race and has never been diagnosed with any type of sever disease particularly any type of cancer.

[0066] In another embodiment, the reference value of expression of ANTXR1 or IFN-I is a value for expression of ANTXR1 or IFN-I that is accepted in the art. This reference value can be baseline value calculated for a group of subjects based on the average or mean values of ANTXR1 or IFN-I expression by applying standard statistically methods.

[0067] In one embodiment, the expression level is determined by a method selected from the group consisting of detecting mRNA of the gene, detecting a protein encoded by the gene, and detecting a biological activity of the protein encoded by the gene.

[0068] In certain aspects of the present invention, the expression level of ANTXR1 or IFN-I is determined in a cancerous sample from a subject. The sample preferably includes tumor cells, any fluid from the surrounding of tumor cells (e.g. leukemic blood, or tumor tissue) or any fluid that is in physiological contact or proximity with the tumor, or any other body fluid in addition to those recited herein should also be considered to be included herein.

[0069] Methods of Measurement

[0070] Any method known to those in the art can be employed for determining the expression level of ANTXR1, IFN-I and/or other biomarkers at the transcriptional or translational level. For example, a microarray can be used. Microarrays are known in the art and consist of a surface to which probes that correspond in sequence to gene products (e.g. mRNAs, polypeptides, fragments thereof etc.) can be specifically hybridized or bound to a known position. To detect at least one gene of interest, a hybridization sample is formed by contacting the test sample with at least one nucleic acid probe. A preferred probe for detecting ANTXR1 and/or IFN-I is a labeled nucleic acid probe capable of hybridizing to ANTXR1 and/or IFN-I

mRNA(s). The nucleic acid probe can be, for example, a full-length nucleic acid molecule, or a portion thereof, such as an oligonucleotide of at least 10, 15, or 20 nucleotides in length and sufficient to specifically hybridize under stringent conditions to the appropriate target. The hybridization sample is maintained under conditions which are sufficient to allow specific hybridization of the nucleic acid probe to a target of interest. Specific hybridization can be performed under high stringency conditions or moderate stringency conditions, as appropriate. In a preferred embodiment, the hybridization conditions for specific hybridization are high stringency. Specific hybridization, if present, is then detected using standard methods. If specific hybridization occurs between the nucleic acid probe and a gene in the test sample, the sequence that is present in the nucleic acid probe is also present in the mRNA of the subject. More than one nucleic acid probe can also be used. Hybridization intensity data detected by the scanner are automatically acquired and processed by the Affymetrix Microarray Suite (MASS) software. Raw data is normalized to expression levels using a target intensity of 150. An alternate method to measure mRNA expression profiles of a small number of different genes is by e.g. either classical TaqMan® Gene Expression Assays or TaqMan® Low Density Array—micro fluidic cards (Applied Biosystems). Particularly, this invention preferably utilizes a qPCR system. Non-limiting examples include commercial kits such as the PrimePCRPathways® commercially available from Bio-rad (Berkley, California).

[0071] The transcriptional state of a sample, particularly mRNAs, may also be measured by other nucleic acid expression technologies known in the art. mRNA can be isolated from the sample using any method known to those in the art. Non-limiting examples include commercial kits, such as the RNeasy® commercially available from Qiagen (Netherlands) or the Mini Kit the TRI Reagent® commercially available from Molecular Research Center, Inc. (Cincinnati, Ohio), can be used to isolate RNA. Generally, the isolated mRNA may be amplified using methods known in the art. Amplification systems utilizing, for example, PCR or RT-PCR methodologies are known to those skilled in the art. For a general overview of amplification technology, see, for example, Dieffenbach *et al.*, PCR Primer: A Laboratory Manual, Cold Spring Harbor Laboratory Press, New York (1995).

[0072] Another accurate method for profiling mRNA expression can the use of Next Generation Sequencing (NGS) including first, second, third as well as subsequent Next Generations Sequencing technologies.

[0073] In other aspects provided herein, determining the amount or detecting the biological activity of a peptide, polypeptide can be achieved by all known means in the art for determining the amount of a peptide or polypeptide in a sample. These means comprise immunoassay devices and methods which may utilize labeled molecules in various sandwich, competition, or other assay formats. Such assays will develop a signal which is indicative for the presence or absence of the peptide or polypeptide. Moreover, the signal strength can, preferably, be correlated directly or indirectly (e.g. reverse- proportional) to the amount of polypeptide present in a sample. Further suitable methods comprise measuring a physical or chemical property specific for the peptide or polypeptide such as its precise molecular mass or NMR spectrum. These methods comprise, preferably, biosensors, optical devices coupled to immunoassays, biochips, analytical devices such as mass- spectrometers, NMR- analyzers, HPLC, FPLC, or chromatography devices. Further, methods include, Western blots, micro-plate ELISA-based methods, fully-automated or robotic immunoassays (available for example on Elecsys™ analyzers), CBA (an enzymatic Cobalt Binding Assay, available for example on Roche-Hitachi™ analyzers), and latex agglutination assays (available for example on Roche-Hitachi™ analyzers).

[0074] In some embodiments, for the various methods disclosed herein, the expression level of ANTXR1 is determined based on the level of an ANTXR1 mRNA or an ANTXR1 protein and the expression level of IFN-I is determined based on the level of an IFN-I biomarker mRNA or an IFN-I biomarker protein. In one embodiment, the IFN-I biomarker mRNA or IFN-I biomarker protein is at least one mRNA or protein selected from the group consisting of IFI35, IFN-α, IFN-β, IFN-κ, IFN-δ, IFN-ε, IFN-τ, IFN-ω, and IFN-ζ, ADAR, IRF9, IFITM3, IFITM2, USP18, LOC144383, EGR1, IFI6, GBP2, HLA-A, HLA-B, HLA-C, HLA-F, HLA-G, IRF8, IFI27, IFI35, IFIT2, IFIT1, IFIT3, IFNA1, IFNA2, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNA10, IFNA14, IFNA16, IFNA17, IFNA21, IFNAR1, IFNAR2, IFNB1, IRF1, IRF2, IRF3, IRF4, IRF5, IRF6, IRF7, ISG20, JAK1, MX1, MX2, OAS1, OAS2, OAS3, IP6K2, XAF1, PSMB8, PTPN1, PTPN6, RNASEL, HLA-K, STAT1, STAT2, TYK2, HLA-B, IFITM1, OASL, SOCS1, SOCS3 and ISG15. In another embodiment, the IFN-I biomarker mRNA or IFN-I biomarker protein is IFI35 mRNA or IFI35 protein.

[0075] Combination Therapies

[0076] The compositions and methods for treating a cancer in a subject using SVV or SVV derivatives described herein may be useful when combined with at least one additional compound useful for treating cancer. The additional compound may comprise a commercially available compound, known to treat, prevent, or reduce the symptoms of cancer and/or metastasis.

[0077] In one aspect, the pharmaceutical composition disclosed herein may be used in combination with a therapeutic agent such as an anti-tumor agent, including but not limited to a chemotherapeutic agent, an anti-cell proliferation agent or any combination thereof. For example, any conventional chemotherapeutic agents of the following non-limiting exemplary classes are included in the invention: alkylating agents; nitrosoureas; antimetabolites; antitumor antibiotics; plant alkyloids; taxanes; hormonal agents; and miscellaneous agents. In another aspect, the pharmaceutical composition disclosed herein may be used in combination with a radiation therapy.

[0078] Most alkylating agents are cell cycle non-specific. In specific aspects, they stop tumor growth by cross-linking guanine bases in DNA double-helix strands. Non-limiting examples include busulfan, carboplatin, chlorambucil, cisplatin, cyclophosphamide, dacarbazine, ifosfamide, mechlorethamine hydrochloride, melphalan, procarbazine, thiotepa, and uracil mustard.

[0079] Anti-metabolites prevent incorporation of bases into DNA during the synthesis (S) phase of the cell cycle, prohibiting normal development and division. Non-limiting examples of antimetabolites include drugs such as 5-fluorouracil, 6-mercaptopurine, capecitabine, cytosine arabinoside, floxuridine, fludarabine, gemcitabine, methotrexate, and thioguanine.

[0080] Antitumor antibiotics generally prevent cell division by interfering with enzymes needed for cell division or by altering the membranes that surround cells. Included in this class are the anthracyclines, such as doxorubicin, which act to prevent cell division by disrupting the structure of the DNA and terminate its function. These agents are cell cycle non-specific. Non-limiting examples of antitumor antibiotics include aclacinomycin, actinomycin, anthramycin, azaserine, bleomycins, cactinomycin, calicheamicin, carubicin, caminomycin, carzinophilin, chromomycin, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin, epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins, mitoxantrone, mycophenolic acid, nogalamycin, olivomycins, peplomycin, porfiromycin,

puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin.

[0081] Plant alkaloids inhibit or stop mitosis or inhibit enzymes that prevent cells from making proteins needed for cell growth. Frequently used plant alkaloids include vinblastine, vincristine, vindesine, and vinorelbine. However, the invention should not be construed as being limited solely to these plant alkaloids.

[0082] The taxanes affect cell structures called microtubules that are important in cellular functions. In normal cell growth, microtubules are formed when a cell starts dividing, but once the cell stops dividing, the microtubules are disassembled or destroyed. Taxanes prohibit the microtubules from breaking down such that the cancer cells become so clogged with microtubules that they cannot grow and divide. Non-limiting exemplary taxanes include paclitaxel and docetaxel.

[0083] Hormonal agents and hormone-like drugs are utilized for certain types of cancer, including, for example, leukemia, lymphoma, and multiple myeloma. They are often employed with other types of chemotherapy drugs to enhance their effectiveness. Sex hormones are used to alter the action or production of female or male hormones and are used to slow the growth of breast, prostate, and endometrial cancers. Inhibiting the production (aromatase inhibitors) or action (tamoxifen) of these hormones can often be used as an adjunct to therapy. Some other tumors are also hormone dependent. Tamoxifen is a non-limiting example of a hormonal agent that interferes with the activity of estrogen, which promotes the growth of breast cancer cells.

[0084] Miscellaneous agents include chemotherapeutics such as bleomycin, hydroxyurea, L-asparaginase, and procarbazine.

[0085] Other examples of chemotherapeutic agents include, but are not limited to, the following and their pharmaceutically acceptable salts, acids and derivatives: MEK inhibitors, such as but not limited to, refametinib, selumetinib, trametinib or cobimetinib; nitrogen mustards such as chlorambucil, chlomaphazine, chlorophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosoureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, ranimustine; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-

azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, 5-FU; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; amsacrine; bestrabucil; bisantrene; edatrexate; defofamine; demecolcine; diaziquone; eflornithine; elliptinium acetate; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidamine; mitoguazone; mitoxantrone; mopidamol; nitracrine; pentostatin; phenamet; pirarubicin; podophyllinic acid; 2-ethylhydrazide; procarbazine; polysaccharide-K (PSK); razoxane; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2′,2″-trichlorotriethylamine; urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxoids, e.g. paclitaxel (TAXOLO, Bristol-Myers Squibb Oncology, Princeton, N.J.) and docetaxel (TAXOTERE, Rhone-Poulenc Rorer, Antony, France); chlorambucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitomycin C; mitoxantrone; vincristine; vinorelbine; navelbine; novantrone; teniposide; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylornithine (DMFO); retinoic acid; esperamicins; and capecitabine.

[0086] An anti-cell proliferation agent can further be defined as an apoptosis-inducing agent or a cytotoxic agent. The apoptosis-inducing agent may be a granzyme, a Bcl-2 family member, cytochrome C, a caspase, or a combination thereof. Exemplary granzymes include granzyme A, granzyme B, granzyme C, granzyme D, granzyme E, granzyme F, granzyme G, granzyme H, granzyme I, granzyme J, granzyme K, granzyme L, granzyme M, granzyme N, or a combination thereof. In other specific aspects, the Bcl-2 family member is, for example, Bax, Bak, Bcl-Xs, Bad, Bid, Bik, Hrk, Bok, or a combination thereof.

[0087] In additional aspects, the caspase is caspase-1, caspase-2, caspase-3, caspase-4, caspase-5, caspase-6, caspase-7, caspase-8, caspase-9, caspase-10, caspase-11, caspase-12, caspase-13, caspase-14, or a combination thereof. In specific aspects, the cytotoxic agent is TNF-α, gelonin, Prodigiosin, a ribosome-inhibiting protein (RIP), *Pseudomonas* exotoxin, *Clostridium difficile* Toxin B, *Helicobacter pylori* VacA, *Yersinia enterocolitica* YopT, Violacein, diethylenetriaminepentaacetic acid, irofulven, Diptheria Toxin, mitogillin, ricin, botulinum toxin, cholera toxin, saporin 6, or a combination thereof.

[0088] An immunotherapeutic agent may be, but is not limited to, an interleukin-2 or other cytokine, an inhibitor of programmed cell death protein 1 (PD-1) signaling such as a monoclonal antibody that binds to PD-1, Ipilimumab. The immunotherapeutic agent can also block cytotoxic T lymphocytes associated antigen A-4 (CTLA-4) signaling and it can also relate to cancer vaccines and dendritic cell-based therapies.

[0089] In one embodiment the subject suffering from cancer is administered at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a dendritic cell-based therapy, a cancer vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative and a combination of any thereof. In one embodiment, the least one anti-cancer therapeutic agent is administered formerly, simultaneously or subsequently to the administering of the SVV or SVV derivative.

[0090] In one embodiment, the subject is administered an IFN-I inhibiting agent. The IFN-I inhibiting agent used herein encompasses any agent known in the art for inhibiting, suppressing or reducing partially or fully and temporarily or permanently IFN type I pathway.

[0091] The inhibiting agent comprises siRNA, ribozyme, an antisense molecule, an aptamer, a peptidomimetic, a small molecule, histone deacetylase (HDAC) inhibitor, Janus kinase (JAK) inhibitor, IFN inhibitor, IFN antibody, IFN-α Receptor 1 antibody, IFN-α Receptor 2 antibody and viral peptide and a combination of any thereof. The viral peptide can be, but not limited to, NS1 protein from an Influenza virus or NS2B3 protease complex from dengue virus.

[0092] A large number of HDAC inhibitors are known and used in the art. The most common HDAC inhibitors bind to the zinc-containing catalytic domain of the HDACs. These HDAC inhibitors can be classified into several groupings named according to their chemical structure and the chemical moiety that binds to the zinc ion. Some examples include, but are not limited to, hydroxamic acids or hydroxamates (such as Trichostatin A or Vorinostat/SAHA (FDA approved)), aminobenzamides Entinostat (MS-275), Tacedinaline (CI994), and Mocetinostat (MGCD0103), cyclic peptides (Apicidin, Romidepsin (FDA approved)), cyclic tetrapeptides or epoxyketones (such as Trapoxin B), depsipeptides, benzamides, electrophilic

ketones, and carboxylic aliphatic acid compounds (such as butyrate, phenylbutyrate, valproate and valproic acid). Other HDAC inhibitors include, but are not limited not, Belinostat (PXD101), LAQ824, and Panobinostat (LBH589). Examples of HDCA inhibitors in clinical trials include Panobinostat (LBH-589), Belinostat (PXD101), Entinostat (MS275), Mocetinostat (MGCD01030), Givinostat (ITF2357), Practinostat (SB939), Chidamide (CS055/HBI-8000), Quisinostat (JNJ-26481585), Abexinostat (PCI-24781), CHR-3996 and AR-Z2.

[0093] JAK inhibitors inhibit the activity of one or more of the Janus kinase family of enzymes (e.g. JAK1, JAK2, JAK3 and/or TYK2), thereby interfering with the JAK-STAT signaling pathway. Various JAK inhibitors are known and used in the art for the treatment of inflammatory diseases or cancer. Non-limiting examples of JAK inhibitors are FDA approved compounds including Ruxolitinib (Jakafi/Jakavi), Tofacitinib (Jakvinus, formerly known as tasocitinib and CP-690550), Oclacitinib (Apoquel), Baricitinib (Olumiant, LY3009104), Decernotinib (VX-509). Other JAK inhibitors are under clinical trials and/or used as experimental drugs. These include for instance Filgotinib (G-146034, GLPG-0634), Cerdulatinib (PRT062070), Gandotinib (LY-2784544), Lestaurtinib (CEP-701), Momelotinib (GS-0387, CYT-387), Pacritinib (SB1518), PF-04965842, Upadacitinib (ABT-494), Peficitinib (ASP015K, JNJ-54781532), Fedratinib (SAR302503), Cucurbitacin I, CHZ868, ABT-494, dimethyl fumarate (DMF, Tecfidera), GLPG0634, and CEP-33779.

[0094] In one embodiment, the subject is administered at least one IFN-I inhibiting agent selected from the group consisting of: HDAC inhibitor, JAK inhibitor, IFN inhibitor, IFN antibody, IFN-α Receptor 1 antibody, IFN-α Receptor 2 antibody and viral peptide and a combination of any thereof. In another embodiment, the at least one IFN-I inhibiting agent is administered formerly, simultaneously or subsequently to the administering of the SVV or SVV derivative. In some embodiments, the at least one IFN-I inhibiting agent is subsequently removed once the SVV has replicated in the tumor cells and before the addition of an anti-cancer therapeutic agent (e.g. checkpoint inhibitor).

[0095] In one embodiment, the anti-cancer therapeutic agent is administered formerly, simultaneously or subsequently to the administering of the at least one IFN-I inhibiting agent. In one embodiment, the anti-cancer therapeutic agent is administered subsequently to the administering of the at least one IFN-I inhibiting agent. In another embodiment, the anti-cancer

therapeutic agent is administered subsequently to the administering of the at least one IFN-I inhibiting agent and the SVV or SVV derivative.

[0096] In one embodiment the SVV or SVV derivative treatment is preceded by the administration of IFN-I inhibiting agent. In one embodiment, once SVV replication and cancer cells death are confirmed, the administration of IFN-I inhibiting agent is terminated. For instance, cancer cells can be treated with an IFN-I inhibitor, (e.g. (5-(tetradecyloxy)-2-furoic acid), acetyl-CoA carboxylase inhibitor: TOFA), 24 hours before SVV treatment and then both treatments can be pursued for several weeks until robust SVV replication is observed and markers of cell death are detected. Then the treatment with IFN-I inhibiting agent can be terminated and an anti-cancer therapeutic agent (such as but not limited to a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor or a CTLA-4 inhibitor) can be initiated. Upon SVV replication, various nucleic acids and cellular debris are generated which can trigger the activation of an influx of immune cells (e.g. T-cells, NK, cells, APCs, etc.) to proceed in cancer cells killing and this process of immune response is enhanced further by the termination of IFN-I inhibition.

[0097] Pharmaceutical Compositions and Formulations.

[0098] Also provided herein is the use of a pharmaceutical composition comprising an SVV or an SVV derivative depleting agent for use in the methods of the invention.

[0099] Such a pharmaceutical composition is in a form suitable for administration to a subject, or the pharmaceutical composition may further comprise one or more pharmaceutically acceptable carriers, one or more additional ingredients, or some combination of these. The various components of the pharmaceutical composition may be present in the form of a physiologically acceptable salt, such as in combination with a physiologically acceptable cation or anion, as is well known in the art.

[00100] In an embodiment provided herein, the pharmaceutical composition useful for practicing the method of the invention may be administered to deliver a dose of between 1 ng/kg/day and 100 mg/kg/day. In another embodiment, the pharmaceutical composition useful for practicing the invention may be administered to deliver a dose of between 1 ng/kg/day and 500 mg/kg/day. The relative amounts of the active ingredient, the pharmaceutically acceptable carrier, and any additional ingredients in a pharmaceutical composition of the invention will vary, depending upon the identity, size, and condition of the subject treated and further

depending upon the route by which the composition is to be administered. By way of example, the composition may comprise between 0.1% and 100% (w/w) active ingredient.

[00101] Pharmaceutical compositions that are useful in the methods of the invention may be suitably developed for inhalational, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal, ophthalmic, intrathecal, intravenous or another route of administration. Other contemplated formulations include projected nanoparticles, liposomal preparations, resealed erythrocytes containing the active ingredient, and immunologically-based formulations. The route(s) of administration is readily apparent to the skilled artisan and depends upon any number of factors including the type and severity of the disease being treated, the type and age of the veterinary or human patient being treated, and the like.

[00102] The formulations of the pharmaceutical compositions described herein may be prepared by any method known or hereafter developed in the art of pharmacology. In general, such preparatory methods include the step of bringing the active ingredient into association with a carrier or one or more other accessory ingredients, and then, if necessary or desirable, shaping or packaging the product into a desired single- or multi-dose unit. In some embodiments, the SVV or derivative thereof can be formulated in a natural capsid, a modified capsid, as a naked RNA, or encapsulated in a protective coat.

[00103] The amount of the active ingredient is generally equal to the dosage of the active ingredient that would be administered to a subject or a convenient fraction of such a dosage such as, for example, one-half or one-third of such a dosage. The unit dosage form may be for a single daily dose or one of multiple daily doses (*e.g.*, about 1 to 4 or more times per day). When multiple daily doses are used, the unit dosage form may be the same or different for each dose.

[00104] Although the descriptions of pharmaceutical compositions provided herein are principally directed to pharmaceutical compositions suitable for ethical administration to humans, it is understood by the skilled artisan that such compositions are generally suitable for administration to animals of all sorts. Modification of pharmaceutical compositions suitable for administration to humans in order to render the compositions suitable for administration to various animals is well understood, and the ordinarily skilled veterinary pharmacologist can design and perform such modification with merely ordinary, if any, experimentation. Subjects to which administration of the pharmaceutical compositions of the invention is contemplated

include, but are not limited to, humans and other primates, mammals including commercially relevant mammals such as cattle, pigs, horses, sheep, cats, and dogs. In one embodiment, the subject is a human or a non-human mammal such as but not limited to an equine, an ovine, a bovine, a porcine, a canine, a feline and a murine. In one embodiment, the subject is a human.

[00105] In one embodiment, the compositions are formulated using one or more pharmaceutically acceptable excipients or carriers. In one aspect a pharmaceutical composition is disclosed for treating a cancer in a subject. The pharmaceutical composition comprises an IFN-I inhibiting agent, an SVV or an SVV derivative and a pharmaceutical acceptable carrier. Pharmaceutically acceptable carriers, which are useful, include, but are not limited to, glycerol, water, saline, ethanol and other pharmaceutically acceptable salt solutions such as phosphates and salts of organic acids. The carrier may be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and vegetable oils. The proper fluidity may be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms may be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. In many cases, it is preferable to include isotonic agents, for example, sugars, sodium chloride, or polyalcohols such as mannitol and sorbitol, in the composition. Prolonged absorption of the injectable compositions may be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate or gelatin.

[00106] Formulations may be employed in admixtures with conventional excipients, i.e., pharmaceutically acceptable organic or inorganic carrier substances suitable for oral, parenteral, nasal, intravenous, subcutaneous, enteral, or any other suitable mode of administration, known to the art. The pharmaceutical preparations may be sterilized and if desired mixed with auxiliary agents, *e.g.*, lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic pressure buffers, coloring, flavoring and/or aromatic substances and the like. They may also be combined where desired with other active agents, e.g., other analgesic agents.

[00107] The disclosed composition may comprise a preservative from about 0.005% to 2.0% by total weight of the composition. The preservative is used to prevent spoilage in the case

of exposure to contaminants in the environment. Examples of preservatives useful in accordance with the invention included but are not limited to those selected from the group consisting of benzyl alcohol, sorbic acid, parabens, imidurea and combinations thereof. A particularly preferred preservative is a combination of about 0.5% to 2.0% benzyl alcohol and 0.05% to 0.5% sorbic acid.

[00108] The composition may include an antioxidant and a chelating agent which inhibit the degradation of the compound. Preferred antioxidants for some compounds are BHT, BHA, alpha-tocopherol and ascorbic acid in the preferred range of about 0.01% to 0.3% and more preferably BHT in the range of 0.03% to 0.1% by weight by total weight of the composition. Preferably, the chelating agent is present in an amount of from 0.01% to 0.5% by weight by total weight of the composition. Particularly preferred chelating agents include edetate salts (e.g. disodium edetate) and citric acid in the weight range of about 0.01% to 0.20% and more preferably in the range of 0.02% to 0.10% by weight by total weight of the composition. The chelating agent is useful for chelating metal ions in the composition which may be detrimental to the shelf life of the formulation. While BHT and disodium edetate are the particularly preferred antioxidant and chelating agent respectively for some compounds, other suitable and equivalent antioxidants and chelating agents may be substituted therefore as would be known to those skilled in the art.

[00109] Administration/Dosing

[00110] The regimen of administration may affect what constitutes an effective amount. For example, the therapeutic formulations may be administered to the patient subject either prior to or after a surgical intervention related to cancer, or shortly after the patient was diagnosed with cancer. Further, several divided dosages, as well as staggered dosages may be administered daily or sequentially, or the dose may be continuously infused, or may be a bolus injection. Further, the dosages of the therapeutic formulations may be proportionally increased or decreased as indicated by the exigencies of the therapeutic or prophylactic situation.

[00111] Administration of the compositions of the present invention to a patient subject, preferably a mammal, more preferably a human, may be carried out using known procedures, at dosages and for periods of time effective to treat cancer in the subject. An effective amount of the therapeutic compound necessary to achieve a therapeutic effect may vary according to factors such as the activity of the particular compound employed; the time of

administration; the rate of excretion of the compound; the duration of the treatment; other drugs, compounds or materials used in combination with the compound; the state of the disease or disorder, age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well-known in the medical arts. Dosage regimens may be adjusted to provide the optimum therapeutic response. For example, several divided doses may be administered daily or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation. A non-limiting example of an effective dose range for a therapeutic compound of the invention is from about 0.01 and 50 mg/kg of body weight/per day.

[00112] The compound can be administered to a subject as frequently as several times daily, or it may be administered less frequently, such as once a day, once a week, once every two weeks, once a month, or even less frequently, such as once every several months or even once a year or less. It is understood that the amount of compound dosed per day may be administered, in non-limiting examples, every day, every other day, every 2 days, every 3 days, every 4 days, or every 5 days. For example, with every other day administration, a 5 mg per day dose may be initiated on Monday with a first subsequent 5 mg per day dose administered on Wednesday, a second subsequent 5 mg per day dose administered on Friday, and so on. The frequency of the dose is readily apparent to the skilled artisan and depends upon any number of factors, such as, but not limited to, the type and severity of the disease being treated, and the type and age of the animal. Actual dosage levels of the active ingredients in the pharmaceutical compositions of this invention may be varied so as to obtain an amount of the active ingredient that is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient. A medical doctor, e.g., physician or veterinarian, having ordinary skill in the art may readily determine and prescribe the effective amount of the pharmaceutical composition required. For example, the physician or veterinarian could start doses of the compounds of the invention employed in the pharmaceutical composition at levels lower than that required in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved.

[00113] In particular embodiments, it is especially advantageous to formulate the compound in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the patients to be treated; each unit containing a predetermined quantity of therapeutic compound calculated to

produce the desired therapeutic effect in association with the required pharmaceutical vehicle. The dosage unit forms of the invention are dictated by and directly dependent on (a) the unique characteristics of the therapeutic compound and the particular therapeutic effect to be achieved, and (b) the limitations inherent in the art of compounding/formulating such a therapeutic compound for the treatment of cancer in a patient.

[00114] Routes of Administration

[00115] One skilled in the art will recognize that although more than one route can be used for administration, a particular route can provide a more immediate and more effective reaction than another route.

[00116] Routes of administration of the disclosed compositions include inhalational, oral, nasal, rectal, parenteral, sublingual, transdermal, transmucosal (e.g., sublingual, lingual, (trans)buccal, (trans)urethral, vaginal (e.g., trans- and perivaginally), (intra)nasal, and (trans)rectal), intravesical, intrapulmonary, intraduodenal, intragastrical, intrathecal, subcutaneous, intramuscular, intradermal, intra-arterial, intravenous, intrabronchial, inhalation, and topical administration. Suitable compositions and dosage forms include, for example, tablets, capsules, caplets, pills, gel caps, troches, dispersions, suspensions, solutions, syrups, granules, beads, transdermal patches, gels, powders, pellets, magmas, lozenges, creams, pastes, plasters, lotions, discs, suppositories, liquid sprays for nasal or oral administration, dry powder or aerosolized formulations for inhalation, compositions and formulations for intravesical administration and the like. It should be understood that the formulations and compositions that would be useful in the present invention are not limited to the particular formulations and compositions that are described herein. In one embodiment, the SVV or SVV derivative treatment comprises an administration route selected from the group consisting of inhalation, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal, ophthalmic, intra-hepatic arterial, intrapleural, intrathecal, intra-tumoral, intravenal and any combination thereof.

[00117] In yet another aspect, also provided herein is a kit for determining a predisposition of an efficacious response to an SVV or an SVV derivative based treatment of a cancer in a subject, the kit comprising a reagent for determining the expression level of ANTXRl and a reagent for determining the expression level of IFN-I in the cancer from the subject.

[00118] Kit

[00119] The invention includes a set of preferred oligomers or antibodies, either labeled (e.g., fluorescer, quencher, etc.) or unlabeled, that are useful for the detection of at least ANTXR1 and/or IFN-I.

[00120] In certain embodiments, a kit is provided. Commercially available kits for use in these methods are, in view of this specification, known to those of skill in the art. In general, kits will comprise a detection reagent that is suitable for detecting the presence of a polypeptide or nucleic acid, or mRNA of interest.

[00121] In another embodiment, there is a panel of probe sets or antibodies. Preferred probe sets are designed to detect the expression level of ANTXR1 and/or IFN-I and provide information about the efficacy of an SVV or an SVV derivative based cancer treatment. Probe sets are particularly useful because they are smaller and cheaper than probe sets that are intended to detect as many polynucleotides or peptides as possible in a particular genome. As provided herein, the probe sets are targeted at the detection of polynucleotides or polypeptides that are informative about ANTXR1 and/or IFN-I in cancer cells or tissues. Probe sets may also comprise a large or small number of probes that detect polynucleotides or peptides that are not informative about cancer. Such probes are useful as controls and for normalization (e.g., spiked-in markers). Probe sets may be a dry mixture or a mixture in solution. In some embodiments, probe sets can be affixed to a solid substrate to form an array of probes. The probes may be antibodies, or nucleic acids (e.g., DNA, RNA, chemically modified forms of DNA and RNA), LNAs (Locked nucleic acids), or PNAs (Peptide nucleic acids), or any other polymeric compound capable of specifically interacting with the peptides or nucleic acid sequences of interest.

[00122] It is contemplated that kits may be designed for isolating and/or detecting peptides (e.g. ANTXR1, know cancer markers, immune activators or apoptotic proteins) or nucleic acid sequences in essentially any sample (e.g., leukemic blood, tumor cells, tumor tissue, etc...), and a wide variety of reagents and methods are, in view of this specification, known in the art.

[00123] In further embodiments a kit is provided for treating or ameliorating a cancer, as described elsewhere herein wherein the kit comprises: a) a compound or compositions as described herein; and b) an additional agent or therapy as described herein. The kit can further include instructions or a label for using the kit to treat or ameliorate the cancer. In yet other embodiments, the invention extends to kits assays for a given cancer (such as, but not limited to,

small-cell lung cancer or triple negative breast cancer), as described herein. Such kits may, for example, contain the reagents from PCR or other nucleic acid hybridization technology (microarrays) or reagents for immunologically based detection techniques (e.g., ELISpot, ELISA).

ILLUSTRATIVE EMBODIMENTS

[00124] Provided here are illustrative embodiments of the disclosed technology. These embodiments are illustrative only and do not limit the scope of the present disclosure or of the claims attached

[00125] Embodiment 1. A method of treating a cancer in a subject in need thereof, the method comprising administering to the subject an effective amount of Seneca Valley Virus (SVV) or SVV derivative, wherein the cancer is characterized by: an expression level of anthrax toxin receptor 1 (ANTXRl) higher than an ANTXRl reference value, and an expression level of interferon type I (IFN-I) lower than an IFN-I reference value, wherein the subject is also administered at least one IFN-I inhibiting comprising a JAK inhibitor.

[00126] Embodiment 2. The method of embodiment 1, wherein the expression level of ANTXR1 is determined based on the level of an ANTXR1 mRNA or an ANTXR1 protein.

[00127] Embodiment 3. The method of embodiment 1, wherein the expression level of IFN-I is determined based on the level of an IFN-I biomarker mRNA or an IFN-I biomarker protein.

[00128] Embodiment 4. The method of embodiment 3, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is at least one mRNA or protein selected from the group consisting of IFI35, IFN-α, IFN-β, IFN-κ, IFN-δ, IFN-ε, IFN-τ, IFN-ω, and IFN-ζ, ADAR, IRF9, IFITM3, IFITM2, USP18, LOC144383, EGR1, IFI6, GBP2, HLA-A, HLA-B, HLA-C, HLA-F, HLA-G, IRF8, IFI27, IFI35, IFIT2, IFIT1, IFIT3, IFNA1, IFNA2, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNA10, IFNA14, IFNA16, IFNA17, IFNA21, IFNAR1, IFNAR2, IFNB1, IRF1, IRF2, IRF3, IRF4, IRF5, IRF6, IRF7, ISG20, JAK1, MX1, MX2, OAS1, OAS2, OAS3, IP6K2, XAF1, PSMB8, PTPN1, PTPN6, RNASEL, HLA-K, STAT1, STAT2, TYK2, HLA-B, IFITM1, OASL, SOCS1, SOCS3 and ISG15.

[00129] Embodiment 5. The method of embodiment 3, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is IFI35 mRNA or IFI35 protein.

[00130] Embodiment 6. The method of embodiment 1, wherein the subject is administered at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a dendritic cell-based therapy, a cancer vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative and a combination of any thereof.

[00131] Embodiment 7. The method of embodiment 5, wherein the least one anti-cancer therapeutic agent is administered formerly, simultaneously or subsequently to the administering of the SVV.

[00132] Embodiment 8. The method of embodiment 1, wherein the least one IFN-I inhibiting agent comprises an HDAC inhibitor, an IFN inhibitor, an IFN antibody, an IFN-α Receptor 1 antibody, an IFN-α Receptor 2 antibody, a viral peptide or a combination of any thereof.

[00133] Embodiment 9. The method of embodiment 8, wherein the least one IFN-I inhibiting agent is administered formerly, simultaneously or subsequently to the administering of the SVV.

[00134] Embodiment 10. The method of embodiment 1, wherein the administering comprises an administration route is selected from the group consisting of inhalation, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal, ophthalmic, intra-hepatic arterial, intrathecal, intra-tumoral, intravenal and any combination thereof.

[00135] Embodiment 11. The method of embodiment 1, wherein the cancer comprises a triple negative breast cancer, a small cell lung cancer, a non-small cell lung cancer, a non-small cell squamous carcinoma, an adenocarcinoma, a glioblastoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial cancer, a neuroendocrine cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

[00136] Embodiment 12. A method of treating a cancer in a subject in need thereof, the method comprising administering to the subject an IFN-I inhibiting agent comprising a JAK inhibitor and an effective amount of SVV or SVV derivative, wherein the cancer is characterized

by an expression level of ANTXRl higher than an ANTXRl reference value, and wherein the IFN-I inhibiting agent reduces the expression level of IFN-I in the cancer thereby favoring replication of the SVV or the SVV derivative and killing of the cancer.

[00137] Embodiment 13. The method of embodiment 12, wherein the IFN-I inhibiting agent comprises an HDAC inhibitor, an IFN inhibitor, an IFN antibody, an IFN-α Receptor 1 antibody, an IFN-α Receptor 2 antibody, a viral peptide or a combination of any thereof.

[00138] Embodiment 14. The method of embodiment 12, wherein the IFN-I inhibiting agent is administered formerly, simultaneously or subsequently to the administering of the SVV.

[00139] Embodiment 15. The method of embodiment 12, wherein the expression level of ANTXR1 is determined based on the level of an ANTXR1 mRNA or an ANTXR1 protein.

[00140] Embodiment 16. The method of embodiment 12, wherein the expression level of IFN-I is determined based on the level of an IFN-I biomarker mRNA or an IFN-I biomarker protein.

[00141] Embodiment 17. The method of embodiment 16, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is at least one mRNA or protein selected from the group consisting of IFI35, IFN-α, IFN-β, IFN-κ, IFN-δ, IFN-ε, IFN-τ, IFN-ω, and IFN-ζ, ADAR, IRF9, IFITM3, IFITM2, USP18, LOC144383, EGR1, IFI6, GBP2, HLA-A, HLA-B, HLA-C, HLA-F, HLA-G, IRF8, IFI27, IFI35, IFIT2, IFIT1, IFIT3, IFNA1, IFNA2, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNA10, IFNA14, IFNA16, IFNA17, IFNA21, IFNAR1, IFNAR2, IFNB1, IRF1, IRF2, IRF3, IRF4, IRF5, IRF6, IRF7, ISG20, JAK1, MX1, MX2, OAS1, OAS2, OAS3, IP6K2, XAF1, PSMB8, PTPN1, PTPN6, RNASEL, HLA-K, STAT1, STAT2, TYK2, HLA-B, IFITM1, OASL, SOCS1, SOCS3 and ISG15.

[00142] Embodiment 18. The method of embodiment 16, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is IFI35 mRNA or IFI35 protein.

[00143] Embodiment 19. The method of embodiment 12, wherein the subject is administered at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a

dendritic cell-based therapy, a cancer vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative a combination of any thereof.

[00144] Embodiment 20. The method of embodiment 18, wherein the least one anti-cancer therapeutic agent is administered formerly, simultaneously or subsequently to the administering of the IFN-I inhibiting agent and SVV.

[00145] Embodiment 21. The method of embodiment 12, wherein the administering comprises an administration route is selected from the group consisting of inhalation, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal, ophthalmic, intra-hepatic arterial, intrathecal, intra-tumoral, intravenal and any combination thereof.

[00146] Embodiment 22. The method of embodiment 12, wherein the cancer comprises a triple negative breast cancer, a small cell lung cancer, a non-small cell lung cancer, a non-small cell squamous carcinoma, an adenocarcinoma, a glioblastoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial cancer, a neuroendocrine cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

[00147] Embodiment 23. A method of predicting the efficacy of a cancer treatment comprising an Seneca Valley Virus (SVV), or an SVV derivative, combined with at least one IFN-I inhibiting agent comprising a JAK inhibitor, the method comprising determining the expression level of ANTXRl and the expression level of IFN-I in the cancer from a subject, wherein: an expression level of ANTXRl higher than an ANTXRl reference value, and an expression level of IFN-I lower than an IFN-I reference value are predictive that the treatment is effective, and wherein when the treatment is predicted to be effective, recommending treatment of the subject.

[00148] Embodiment 24. The method of embodiment 23, wherein the expression level of ANTXR1 is determined based on the level of an ANTXR1 mRNA or an ANTXR1 protein.

[00149] Embodiment 25. The method of embodiment 23, wherein the expression level of IFN-I is determined based on the level of an IFN-I biomarker mRNA or an IFN-I biomarker protein.

[00150] Embodiment 26. The method of embodiment 25, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is at least one mRNA or protein selected from the group consisting of IFI35, IFN-α, IFN-β, IFN-κ, IFN-δ, IFN-ε, IFN-τ, IFN-ω, and IFN-ζ, ADAR, IRF9,

IFITM3, IFITM2, USP18, LOC144383, EGR1, IFI6, GBP2, HLA-A, HLA-B, HLA-C, HLA-F, HLA-G, IRF8, IFI27, IFI35, IFIT2, IFIT1, IFIT3, IFNA1, IFNA2, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNA10, IFNA14, IFNA16, IFNA17, IFNA21, IFNAR1, IFNAR2, IFNB1, IRF1, IRF2, IRF3, IRF4, IRF5, IRF6, IRF7, ISG20, JAK1, MX1, MX2, OAS1, OAS2, OAS3, IP6K2, XAF1, PSMB8, PTPN1, PTPN6, RNASEL, HLA-K, STAT1, STAT2, TYK2, HLA-B, IFITM1, OASL, SOCS1, SOCS3 and ISG15.

[00151] Embodiment 27. The method of embodiment 25, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is IFI35 mRNA or IFI35 protein.

[00152] Embodiment 28. The method of embodiment 23, wherein the SVV or SVV derivative treatment further comprises a treatment with at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a dendritic cell-based therapy, a cancer vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative and a combination of any thereof.

[00153] Embodiment 29. The method of embodiment 27, wherein the treatment with at least one anti-cancer therapeutic agent is performed formerly, simultaneously or subsequently to the SVV or SVV derivative treatment.

[00154] Embodiment 30. The method of embodiment 23, wherein the at least one IFN-I inhibiting agent comprises an HDAC inhibitor, a JAK inhibitor, an IFN inhibitor, an IFN antibody, an IFN-α Receptor 1 antibody, an IFN-α Receptor 2 antibody, a viral peptide or a combination of any thereof.

[00155] Embodiment 31. The method of embodiment 30, wherein the least one IFN-I inhibiting agent is administered formerly, simultaneously or subsequently to the SVV or SVV derivative treatment.

[00156] Embodiment 32. The method of embodiment 23, wherein SVV or SVV derivative treatment comprises an administration route selected from the group consisting of inhalation, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal,

ophthalmic, intra-hepatic arterial, intrathecal, intra-tumoral, intravenal and any combination thereof.

[00157] Embodiment 33. The method of embodiment 23, wherein the cancer comprises a triple negative breast cancer, a small cell lung cancer, a non-small cell lung cancer, a non-small cell squamous carcinoma, an adenocarcinoma, a glioblastoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial cancer, a neuroendocrine cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

[00158] Embodiment 34. A pharmaceutical composition for treating a cancer in a subject, the pharmaceutical composition comprising an IFN-I inhibiting agent comprising a JAK inhibitor, an SVV or an SVV derivative and a pharmaceutical acceptable carrier.

[00159] Embodiment 35. The composition of embodiment 34, wherein the IFN-I inhibiting agent is at least one agent selected from the group consisting of: HDAC inhibitor, JAK inhibitor, IFN inhibitor, IFN antibody, IFN-α Receptor 1 antibody, IFN-α Receptor 2 antibody and viral peptide and a combination of any thereof.

[00160] Embodiment 36. The composition of embodiment 34, further comprises at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a dendritic cell-based therapy, a cancer vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative and a combination of any thereof.

[00161] Embodiment 37. The composition of embodiment 34, wherein the cancer comprises a triple negative breast cancer, small cell lung cancer, a non-small squamous cell carcinoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

[00162] Embodiment 38. A kit for determining a predisposition of an efficacious response to a cancer treatment comprising an Seneca Valley Virus (SVV), or an SVV derivative, combined with at least one IFN-I inhibiting agent comprising a JAK inhibitor, the kit comprising

a reagent for determining the expression level of ANTXR1 and a reagent for determining the expression level of IFN-I in the cancer from a subject.

[00163] Embodiment 39. The method or kit of any one of embodiments 1, 12, 23, 34 and 38, wherein the subject is a human.

[00164] Embodiment 40. A Seneca Valley Virus (SVV) or SVV derivative in combination with at least one IFN-I inhibiting agent comprising a JAK inhibitor for use in the manufacture of a medicament for treatment of a cancer, wherein the cancer is characterized by an expression level of anthrax toxin receptor 1 (ANTXR1) higher than an ANTXR1 reference value, and an expression level of interferon type I (IFN-I) lower than an IFN-I reference value.

EXAMPLES

[00165] The invention is now described with reference to the following Examples. These Examples are provided for the purpose of illustration only and the invention should in no way be construed as being limited to these Examples, but rather should be construed to encompass any and all variations which become evident as a result of the teaching provided herein.

[00166] Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the compounds of the present invention and practice the claimed methods. The following working examples therefore, specifically point out the preferred embodiments of the present invention, and are not to be construed as limiting in any way the remainder of the disclosure.

[00167] Example 1: Importance of ANTXR1 receptor and IFN type I immune pathway for SVV replication

[00168] Immunotherapies, including oncolytic virus therapies alone or in combination with agents known to modulate the tumor microenvironment, are revolutionizing the treatment of cancer, making treatments possible for incurable, hard to target and/or aggressive cancers. The antitumor activity of oncolytic viruses is a consequence of virus associated immunogenic cell death and induction of an immune response against tumor specific antigens.

[00169] Identification and description of ANTXR1/TEM 8 as the cellular receptor for the oncolytic virus SVV in combination with its discrete absence from the surface of normal

healthy cells and presence on the surface of tumor cells and cells within the immediate surrounding environment, makes SVV an ideal candidate for the development of oncolytic virus immunotherapy.

[00170] Genomic analysis of the 42 ANTXR1/TEM 8^{+} cell lines refractory to SVV infection revealed robust expression of RNAs encoding components of the innate immune response. These data suggest that IFN type I (IFN-I) pathway modulates tropism of SVV infection (Miles et al., J Clin Invest.2017; 127(8):2957-2967).

[00171] Several histone deacetylases inhibitors (HDACis) have been approved by the FDA for the treatment of cutaneous/peripheral T-cell lymphomas, hematological malignancies and solid tumors

[00172] Impairing of IFN type I immune pathway will allow for controlled SVV replication in these cells. The amount of IFN-I inhibitor used for impairing the IFN-I pathway may allow maximal replication of SVV and IFN-I inhibition may be reversible upon removal of IFN-I inhibitor.

[00173] Demonstrated herein is a very high correlation (~0.9) between the expression of these two factors above a specific threshold (Figure 18) and permissivity and ability of SVV to efficiently replicate in the cell line. The model fit in Figure 18 through 6-fold cross-validation was used to predict whether a given cell line in the entire set could be permissive based on a minimal interferon gene set using a tuning parameter, lambda, of 0.1.

[00174] Using computational analysis, ANTXR1/TEM 8 was shown to be above the specific threshold in over 60% of solid cancer cell lines in an extensive human cancer cell line database of over 700 cell lines (CCLE) and in the majority of lines in most major solid cancer indications including, but not limited to, triple negative breast cancer, ovarian cancer, NSCLC LC, SCC, adenocarcinoma, endometrial cancer, soft tissue sarcoma, head and neck cancer and bladder cancer. However, the majority of these cancer cell lines had a level of Type I INF gene(s) to predict that they would not be permissive to SVV infection. IFN-I expression, including the entire IFN-I pathway, was shown herein to be efficiently represented by few key biomarkers such as but not limited to biomarker gene IFI35. Other factors that can be relevant for assessing SVV infection and the efficacy of SVV treatment include, but are not limited to, genes involved in SVV cellular entry, uncoating, translation and replication (e.g. TEX2). The results of present analysis highlight the importance of reducing or eliminating, at least

temporarily, IFN-I response to reach a sufficient level of replication of SVV to kill tumor cells by immunogenic cell death and activate an anti-tumor immune response.

[00175] Example 2: SVV administration and combination therapy for cancer treatment

[00176] Contemplated herein is the treatment of patient's tumors in indications known to express above threshold levels of ANTXR1/TEM 8 by multiple intratumoral administration of SVV. This procedure can create a high ratio between the number of SVV infecting viruses and the number of host cancerous cells (high multiplicity of infection (MOI)) and a higher probability of sustained replication, activation of danger signals, immunogenic cells death and induction of an anti-tumor response. Multiple intravenous (IV) administrations at high doses utilizing agents that repress or eliminate the production of neutralizing antibodies can also be considered among others. Further, in order to ensure SVV efficiently replicates, agents known to inhibit, suppress or reduce (temporarily or permanently) IFN-I response can be used to maximize sufficient replication and induce immunogenic cell death and stimulate an anti-tumor immune response.

[00177] Combination of check point inhibitors (CPI) I, IFN-I inhibitors along with SVV may provide the optimal result for cancer treatment as this combination prevents an immune response from the host and favors SVV replication and killing of the cancerous tissue(s).

[00178] Example 3: Positive effect of HDAC inhibitors and JAK inhibitors for SVV cancer cells infection and killing.

[00179] In certain instances, infection with Seneca Valley Virus can be toxic to triple negative breast cancer cell lines. In these cases, it is necessary to reduce innate antiviral responses through the use of certain approved pharmaceutical compounds (see Figure 1, Figure 2 and Figure 5). As shown in Figure 1 and Figure 5, the treatment of HTB-126 cells (triple negative breast cancer cell lines) with Tofacitinib modified and favored the susceptibility to virus mediated killing by SVV. As shown in Figure 2, the treatment of BT-549 cells (triple negative breast cancer cell lines) with Tofacitinib or Vorinostat or Ruxolitinib modified and favored the susceptibility to virus mediated killing by SVV.

[00180] Osteosarcoma cell lines (U2OS) also showed augmented SVV mediated cell killing by similar compounds (e.g. Tofacitinib or Ruxolitinib) that increase cell killing in triple negative breast cancer cell lines (see Figure 3).

[00181] The augmentation of SVV cell killing was also demonstrated in human colorectal cancer cell lines (HCT-116) but the increase in cell killing was mainly caused by HDAC inhibitors (Panobinostat or Vorinostat) instead of the JAK inhibitors (Ruxolitinib, Tofacitinib or Dimethyl fumarate) which modified SVV's killing susceptibility in triple negative breast cancer and osteosarcoma cell lines (see Figure 4).

[00182] The disclosures of each and every patent, patent application, and publication cited herein are hereby incorporated herein by reference in their entirety. While this invention has been disclosed with reference to specific embodiments, it is apparent that other embodiments and variations of this invention may be devised by others skilled in the art without departing from the true spirit and scope of the invention. The appended claims are intended to be construed to include all such embodiments and equivalent variations.

CLAIMS

What is claimed:

1. A method of treating a cancer in a subject in need thereof, the method comprising administering to the subject an effective amount of Seneca Valley Virus (SVV) or SVV derivative, wherein the cancer is characterized by:
    a. an expression level of anthrax toxin receptor 1 (ANTXRl) higher than an ANTXRl reference value, and
    b. an expression level of interferon type I (IFN-I) lower than an IFN-I reference value,

wherein the subject is also administered at least one IFN-I inhibiting agent comprising a JAK inhibitor.

2. The method of claim 1, wherein the expression level of ANTXR1 is determined based on the level of an ANTXR1 mRNA or an ANTXR1 protein.

3. The method of claim 1, wherein the expression level of IFN-I is determined based on the level of an IFN-I biomarker mRNA or an IFN-I biomarker protein.

4. The method of claim 3, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is at least one mRNA or protein selected from the group consisting of IFI35, IFN-α, IFN-β, IFN-κ, IFN-δ, IFN-ε, IFN-τ, IFN-ω, and IFN-ζ, ADAR, IRF9, IFITM3, IFITM2, USP18, LOC144383, EGR1, IFI6, GBP2, HLA-A, HLA-B, HLA-C, HLA-F, HLA-G, IRF8, IFI27, IFI35, IFIT2, IFIT1, IFIT3, IFNA1, IFNA2, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNA10, IFNA14, IFNA16, IFNA17, IFNA21, IFNAR1, IFNAR2, IFNB1, IRF1, IRF2, IRF3, IRF4, IRF5, IRF6, IRF7, ISG20, JAK1, MX1, MX2, OAS1, OAS2, OAS3, IP6K2, XAF1, PSMB8, PTPN1, PTPN6, RNASEL, HLA-K, STAT1, STAT2, TYK2, HLA-B, IFITM1, OASL, SOCS1, SOCS3 and ISG15.

5. The method of claim 3, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is IFI35 mRNA or IFI35 protein.

6. The method of claim 1, wherein the subject is administered at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a dendritic cell-based therapy, a cancer vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative and a combination of any thereof.

7. The method of claim 5, wherein the least one anti-cancer therapeutic agent is administered formerly, simultaneously or subsequently to the administering of the SVV.

8. The method of claim 1, wherein the least one IFN-I inhibiting agent comprises an HDAC inhibitor, an IFN inhibitor, an IFN antibody, an IFN-α Receptor 1 antibody, an IFN-α Receptor 2 antibody, a viral peptide or a combination of any thereof.

9. The method of claim 8, wherein the least one IFN-I inhibiting agent is administered formerly, simultaneously or subsequently to the administering of the SVV.

10. The method of claim 1, wherein the administering comprises an administration route is selected from the group consisting of inhalation, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal, ophthalmic, intra-hepatic arterial, intrathecal, intra-tumoral, intravenal and any combination thereof.

11. The method of claim 1, wherein the cancer comprises a triple negative breast cancer, a small cell lung cancer, a non-small cell lung cancer, a non-small cell squamous carcinoma, an adenocarcinoma, a glioblastoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial cancer, a neuroendocrine cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

12. A method of treating a cancer in a subject in need thereof, the method comprising administering to the subject an IFN-I inhibiting agent comprising a JAK inhibitor and an effective amount of SVV or SVV derivative, wherein the cancer is characterized by an expression level of ANTXRl higher than an ANTXRl reference value, and wherein the IFN-I inhibiting agent reduces the expression level of IFN-I in the cancer thereby favoring replication of the SVV or the SVV derivative and killing of the cancer.

13. The method of claim 12, wherein the IFN-I inhibiting agent comprises an HDAC inhibitor, an IFN inhibitor, an IFN antibody, an IFN-α Receptor 1 antibody, an IFN-α Receptor 2 antibody, a viral peptide or a combination of any thereof.

14. The method of claim 12, wherein the IFN-I inhibiting agent is administered formerly, simultaneously or subsequently to the administering of the SVV.

15. The method of claim 12, wherein the expression level of ANTXR1 is determined based on the level of an ANTXR1 mRNA or an ANTXR1 protein.

16. The method of claim 12, wherein the expression level of IFN-I is determined based on the level of an IFN-I biomarker mRNA or an IFN-I biomarker protein.

17. The method of claim 16, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is at least one mRNA or protein selected from the group consisting of IFI35, IFN-α, IFN-β, IFN-κ, IFN-δ, IFN-ε, IFN-τ, IFN-ω, and IFN-ζ, ADAR, IRF9, IFITM3, IFITM2, USP18, LOC144383, EGR1, IFI6, GBP2, HLA-A, HLA-B, HLA-C, HLA-F, HLA-G, IRF8, IFI27, IFI35, IFIT2, IFIT1, IFIT3, IFNA1, IFNA2, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNA10, IFNA14, IFNA16, IFNA17, IFNA21, IFNAR1, IFNAR2, IFNB1, IRF1, IRF2, IRF3, IRF4, IRF5, IRF6, IRF7, ISG20, JAK1, MX1, MX2, OAS1, OAS2, OAS3, IP6K2, XAF1, PSMB8, PTPN1, PTPN6, RNASEL, HLA-K, STAT1, STAT2, TYK2, HLA-B, IFITM1, OASL, SOCS1, SOCS3 and ISG15.

18. The method of claim 16, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is IFI35 mRNA or IFI35 protein.

19. The method of claim 12, wherein the subject is administered at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a dendritic cell-based therapy, a cancer vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative a combination of any thereof.

20. The method of claim 18, wherein the least one anti-cancer therapeutic agent is administered formerly, simultaneously or subsequently to the administering of the IFN-I inhibiting agent and SVV.

21. The method of claim 12, wherein the administering comprises an administration route is selected from the group consisting of inhalation, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal, ophthalmic, intra-hepatic arterial, intrathecal, intra-tumoral, intravenal and any combination thereof.

22. The method of claim 12, wherein the cancer comprises a triple negative breast cancer, a small cell lung cancer, a non-small cell lung cancer, a non-small cell squamous carcinoma, an adenocarcinoma, a glioblastoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial cancer, a neuroendocrine cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

23. A method of predicting the efficacy of a cancer treatment comprising an Seneca Valley Virus (SVV), or an SVV derivative, combined with at least one IFN-I inhibiting agent comprising a JAK inhibitor, the method comprising determining the expression level of ANTXRl and the expression level of IFN-I in the cancer from a subject, wherein:
    a. an expression level of ANTXRl higher than an ANTXRl reference value, and

b. an expression level of IFN-I lower than an IFN-I reference value

are predictive that the treatment is effective, and wherein when the treatment is predicted to be effective, recommending treatment of the subject.

24. The method of claim 23, wherein the expression level of ANTXR1 is determined based on the level of an ANTXR1 mRNA or an ANTXR1 protein.

25. The method of claim 23, wherein the expression level of IFN-I is determined based on the level of an IFN-I biomarker mRNA or an IFN-I biomarker protein.

26. The method of claim 25, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is at least one mRNA or protein selected from the group consisting of IFI35, IFN-α, IFN-β, IFN-κ, IFN-δ, IFN-ε, IFN-τ, IFN-ω, and IFN-ζ, ADAR, IRF9, IFITM3, IFITM2, USP18, LOC144383, EGR1, IFI6, GBP2, HLA-A, HLA-B, HLA-C, HLA-F, HLA-G, IRF8, IFI27, IFI35, IFIT2, IFIT1, IFIT3, IFNA1, IFNA2, IFNA4, IFNA5, IFNA6, IFNA7, IFNA8, IFNA10, IFNA14, IFNA16, IFNA17, IFNA21, IFNAR1, IFNAR2, IFNB1, IRF1, IRF2, IRF3, IRF4, IRF5, IRF6, IRF7, ISG20, JAK1, MX1, MX2, OAS1, OAS2, OAS3, IP6K2, XAF1, PSMB8, PTPN1, PTPN6, RNASEL, HLA-K, STAT1, STAT2, TYK2, HLA-B, IFITM1, OASL, SOCS1, SOCS3 and ISG15.

27. The method of claim 25, wherein the IFN-I biomarker mRNA or IFN-I biomarker protein is IFI35 mRNA or IFI35 protein.

28. The method of claim 23, wherein the SVV or SVV derivative treatment further comprises a treatment with at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a dendritic cell-based therapy, a cancer

vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative and a combination of any thereof.

29. The method of claim 27, wherein the treatment with at least one anti-cancer therapeutic agent is performed formerly, simultaneously or subsequently to the SVV or SVV derivative treatment.

30. The method of claim 23, wherein the at least one IFN-I inhibiting agent comprises an HDAC inhibitor, a JAK inhibitor, an IFN inhibitor, an IFN antibody, an IFN-α Receptor 1 antibody, an IFN-α Receptor 2 antibody, a viral peptide or a combination of any thereof.

31. The method of claim 30, wherein the least one IFN-I inhibiting agent is administered formerly, simultaneously or subsequently to the SVV or SVV derivative treatment.

32. The method of claim 23, wherein SVV or SVV derivative treatment comprises an administration route selected from the group consisting of inhalation, oral, rectal, vaginal, parenteral, topical, transdermal, pulmonary, intranasal, buccal, ophthalmic, intra-hepatic arterial, intrathecal, intra-tumoral, intravenal and any combination thereof.

33. The method of claim 23, wherein the cancer comprises a triple negative breast cancer, a small cell lung cancer, a non-small cell lung cancer, a non-small cell squamous carcinoma, an adenocarcinoma, a glioblastoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial cancer, a neuroendocrine cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

34. A pharmaceutical composition for treating a cancer in a subject, the pharmaceutical composition comprising an IFN-I inhibiting agent comprising a JAK inhibitor, an SVV or an SVV derivative and a pharmaceutical acceptable carrier.

35. The composition of claim 34, wherein the IFN-I inhibiting agent is at least one agent selected from the group consisting of: HDAC inhibitor, JAK inhibitor, IFN inhibitor, IFN antibody, IFN-α Receptor 1 antibody, IFN-α Receptor 2 antibody and viral peptide and a combination of any thereof.

36. The composition of claim 34, further comprises at least one anti-cancer therapeutic agent selected from the group consisting of: a checkpoint inhibitor, a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a cytokine, a growth factor, a photosensitizing agent, a toxin, a siRNA molecule, a signaling modulator, an anti-cancer antibiotic, an anti-cancer antibody, an angiogenesis inhibitor, a chemotherapeutic compound, anti-metastatic compound, an immunotherapeutic compound, a CAR therapy, a dendritic cell-based therapy, a cancer vaccine, an oncolytic virus, an engineered anti-cancer virus or virus derivative and a combination of any thereof.

37. The composition of claim 34, wherein the cancer comprises a triple negative breast cancer, small cell lung cancer, a non-small squamous cell carcinoma, a skin cancer, a hepatocellular carcinoma, a colon cancer, a cervical cancer, an ovarian cancer, an endometrial cancer, a pancreatic cancer, a thyroid cancer, a kidney cancer, a bone cancer, an oesophagus cancer or a soft tissue cancer.

38. A kit for determining a predisposition of an efficacious response to a cancer treatment comprising an Seneca Valley Virus (SVV), or an SVV derivative, combined with at least one IFN-I inhibiting agent comprising a JAK inhibitor, the kit comprising a reagent for determining the expression level of ANTXRl and a reagent for determining the expression level of IFN-I in the cancer from a subject.

39. The method or kit of any one of claims 1, 12, 23, 34 and 38, wherein the subject is a human.

40. A Seneca Valley Virus (SVV) or SVV derivative in combination with at least one IFN-I inhibiting agent comprising a JAK inhibitor for use in the manufacture of a medicament for treatment of a cancer, wherein the cancer is characterized by an expression level of

anthrax toxin receptor 1 (ANTXRl) higher than an ANTXRl reference value, and an expression level of interferon type I (IFN-I) lower than an IFN-I reference value.

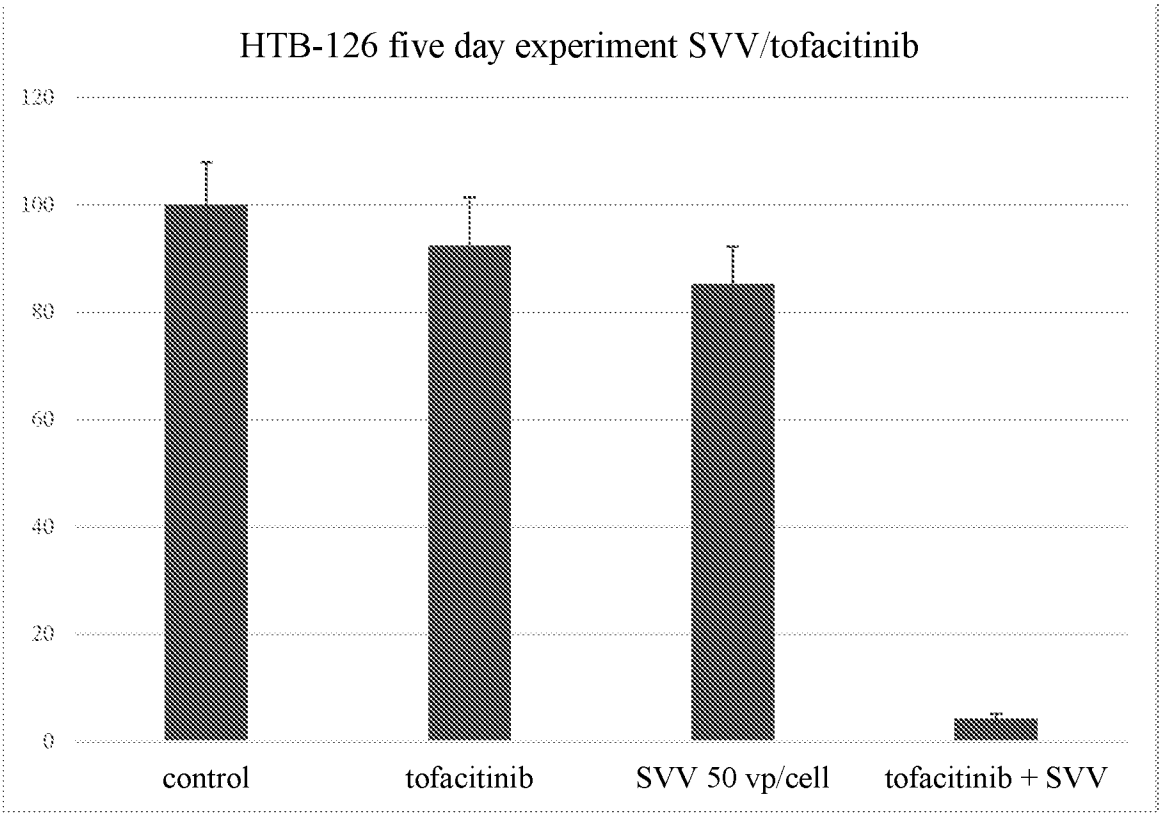

HTB-126 five day experiment SVV/tofacitinib
120
100
80
60
40
20
0
control
tofacitinib
SVV 50 vp/cell
tofacitinib + SVV

Figure 1

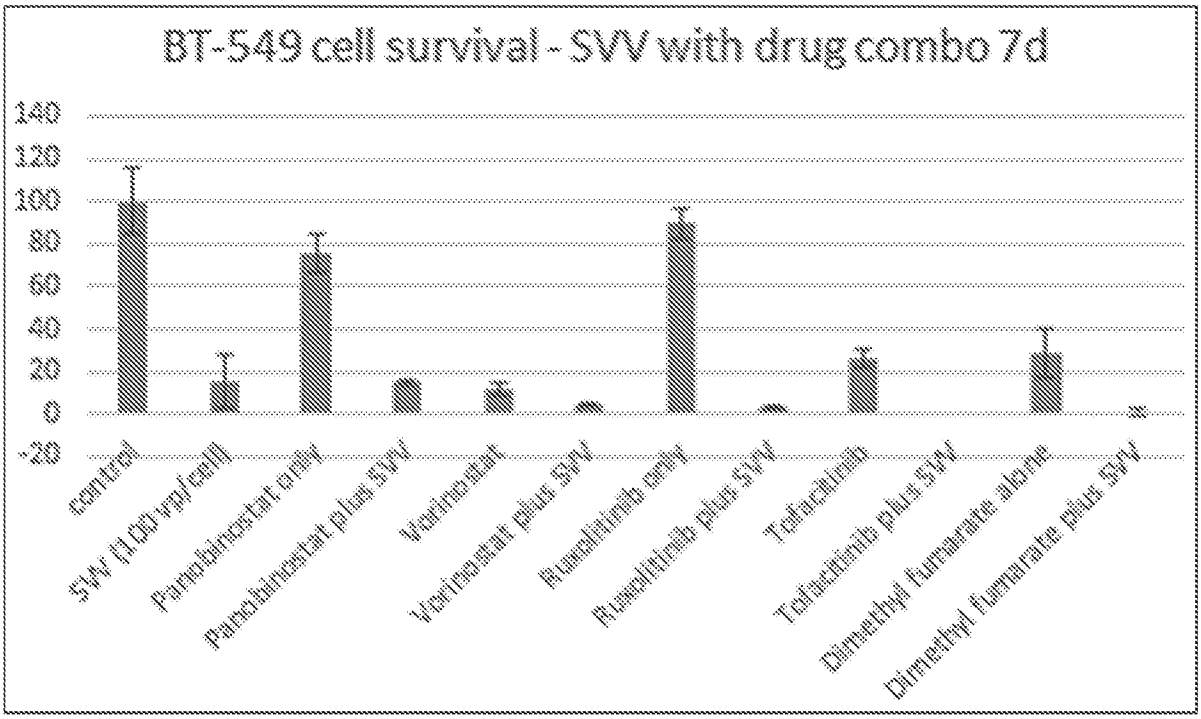

BT-549 cell survival - SVV with drug combo 7d
140
120
100
80
60
40
20
0
-20
control
SVV (1 (10 vp/cell))
Panobinostat only
Panobinostat plus SVV
Vorinostat
Vorinostat plus SVV
Ruxolitinib only
Ruxolitinib plus SVV
Tofacitinib
Tofacitinib plus SVV
Dimethyl fumarate alone
Dimethyl fumarate plus SVV

Figure 2

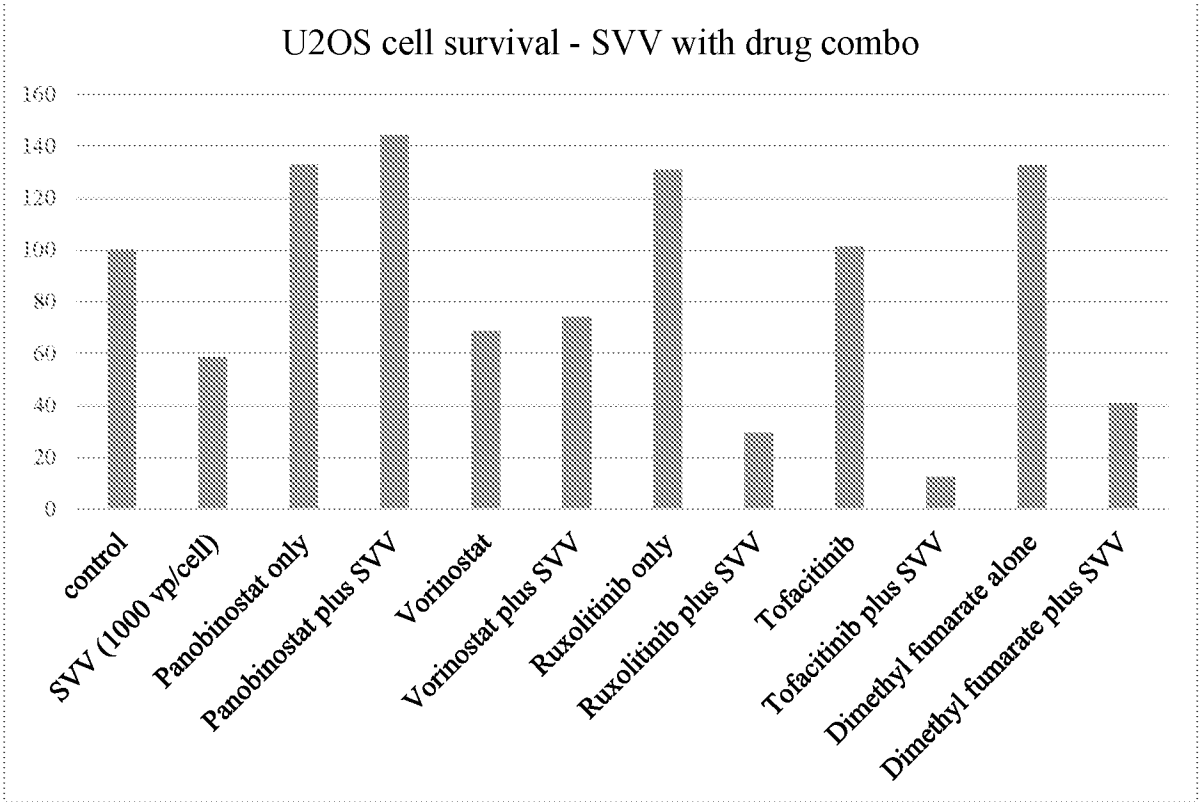

U2OS cell survival - SVV with drug combo
160
140
120
100
80
60
40
20
0
control
SVV (1000 vp/cell)
Panobinostat only
Panobinostat plus SVV
Vorinostat
Vorinostat plus SVV
Ruxolitinib only
Ruxolitinib plus SVV
Tofacitinib
Tofacitinib plus SVV
Dimethyl fumarate alone
Dimethyl fumarate plus SVV

Figure 3

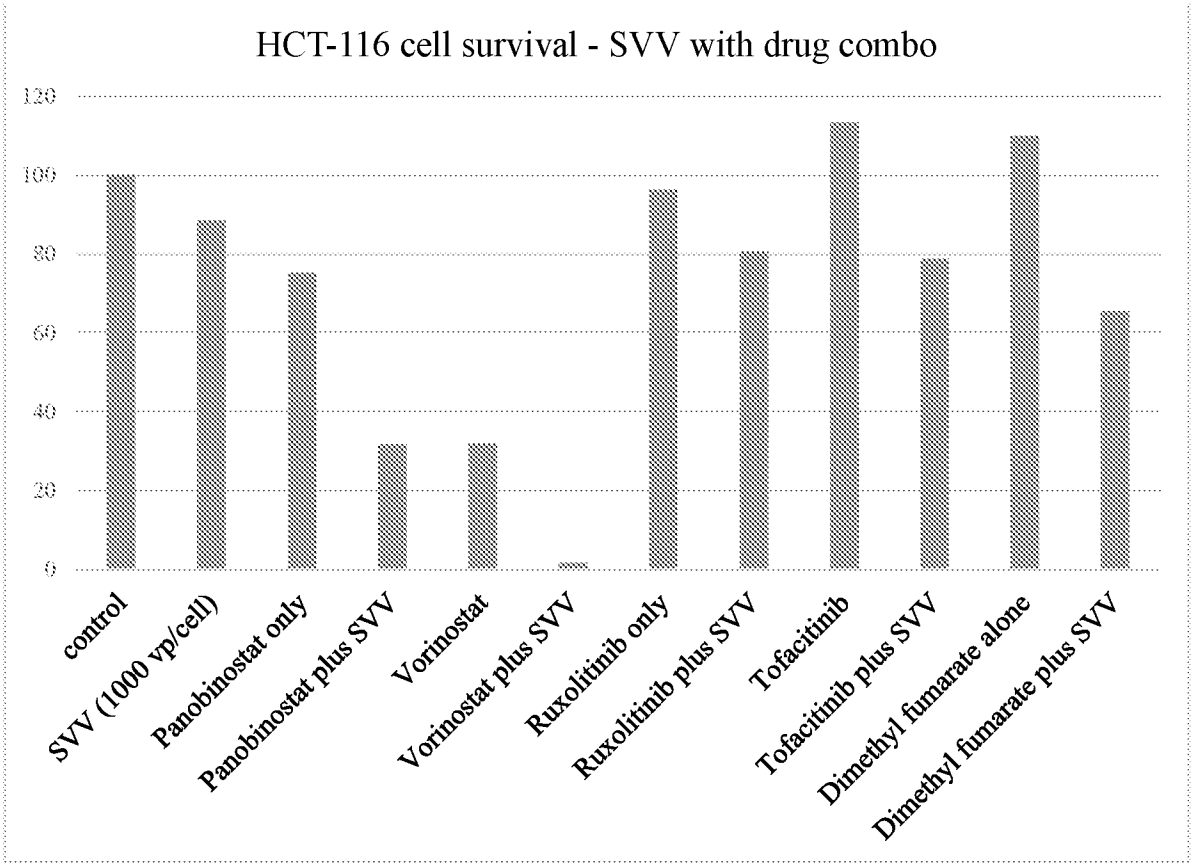

HCT-116 cell survival - SVV with drug combo
120
100
80
60
40
20
0
control
SVV (1000 vp/cell)
Panobinostat only
Panobinostat plus SVV
Vorinostat
Vorinostat plus SVV
Ruxolitinib only
Ruxolitinib plus SVV
Tofacitinib
Tofacitinib plus SVV
Dimethyl fumarate alone
Dimethyl fumarate plus SVV

Figure 4

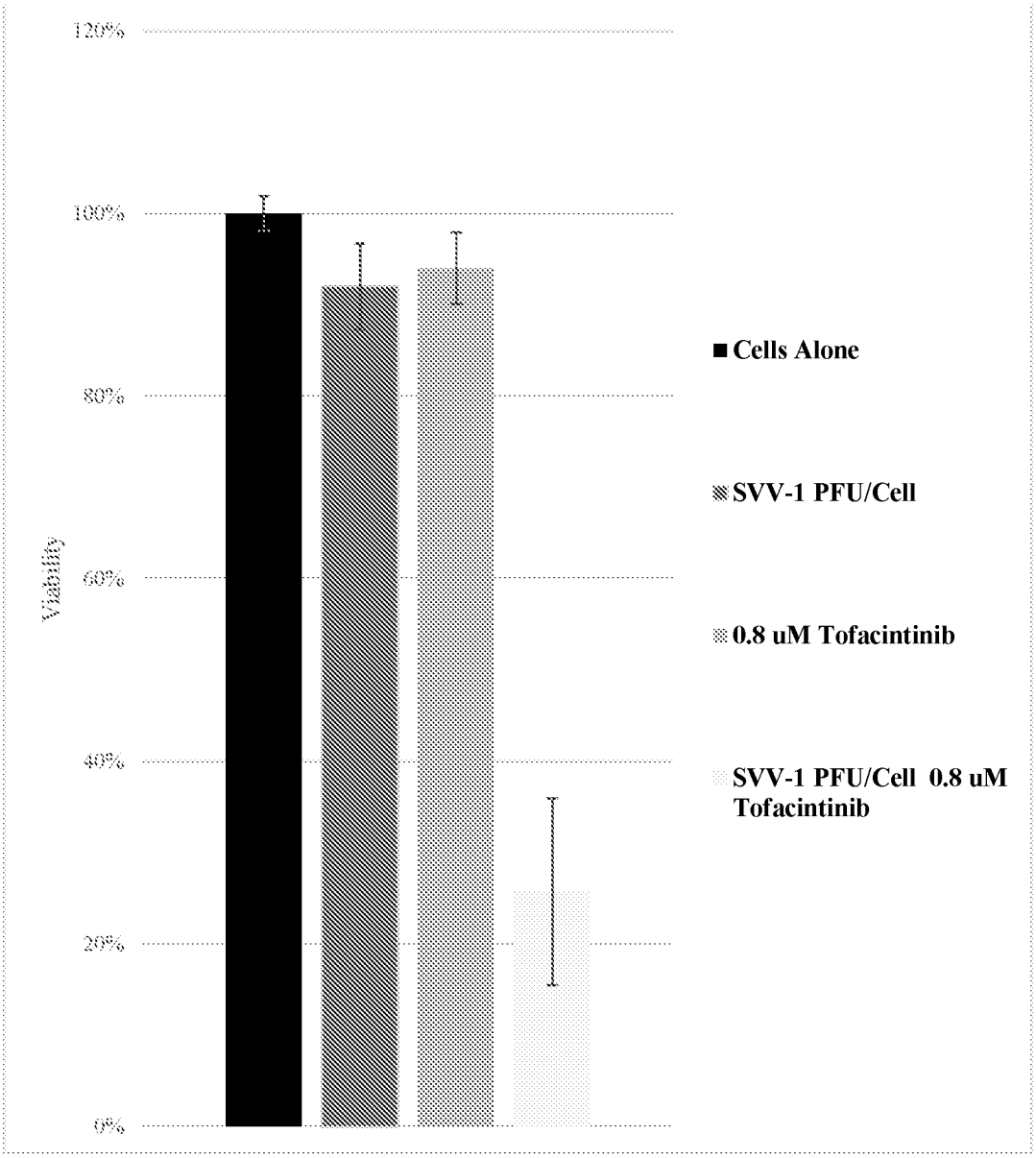

120%
100%
80%
60%
40%
20%
0%
Viability
Cells Alone
SVV-1 PFU/Cell
0.8 uM Tofacintinib
SVV-1 PFU/Cell 0.8 uM Tofacintinib

Figure 5

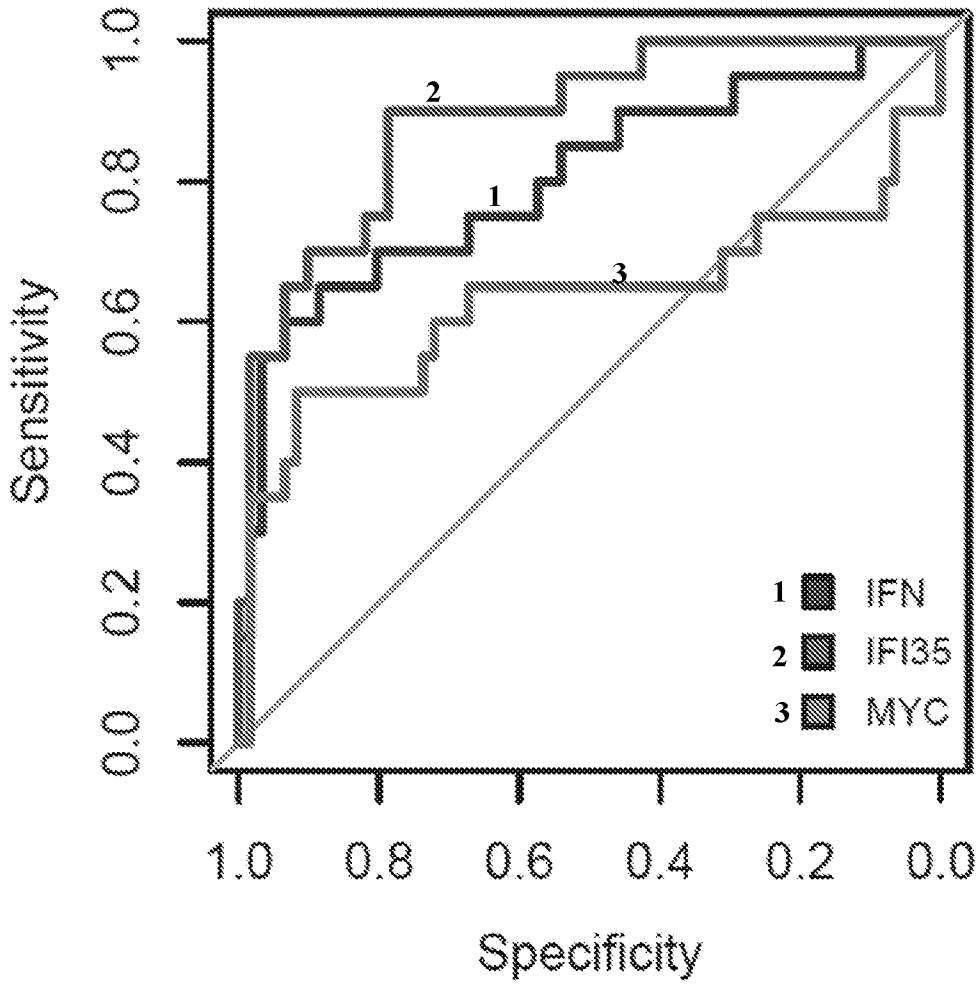

Sensitivity
1.0
0.8
0.6
0.4
0.2
0.0
1.0
0.8
0.6
0.4
0.2
0.0
Specificity
1
2
3
1 IFN
2 IFI35
3 MYC

Figure 6

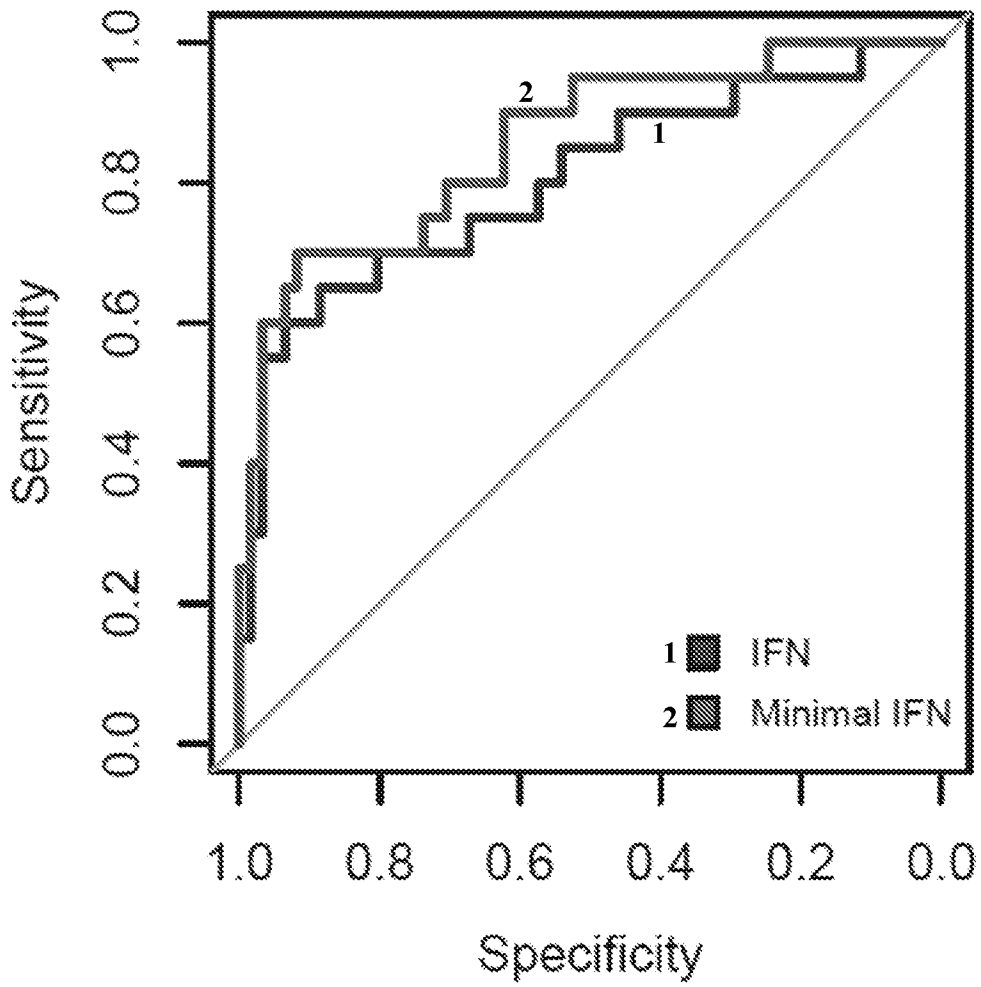

Sensitivity
1.0
0.8
0.6
0.4
0.2
0.0
2
1
1 IFN
2 Minimal IFN
1.0
0.8
0.6
0.4
0.2
0.0
Specificity

Figure 7

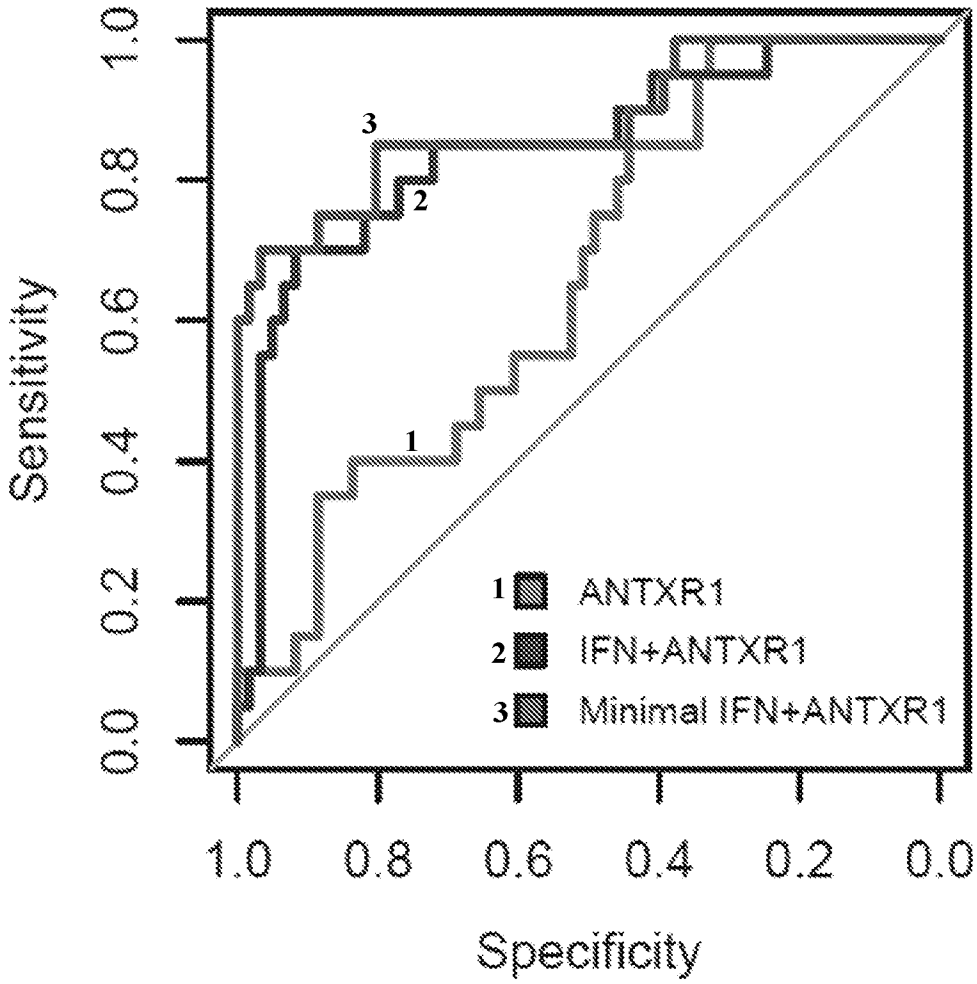

Sensitivity
1.0
0.8
0.6
0.4
0.2
0.0
3
2
1
1 ANTXR1
2 IFN+ANTXR1
3 Minimal IFN+ANTXR1
1.0
0.8
0.6
0.4
0.2
0.0
Specificity

Figure 8

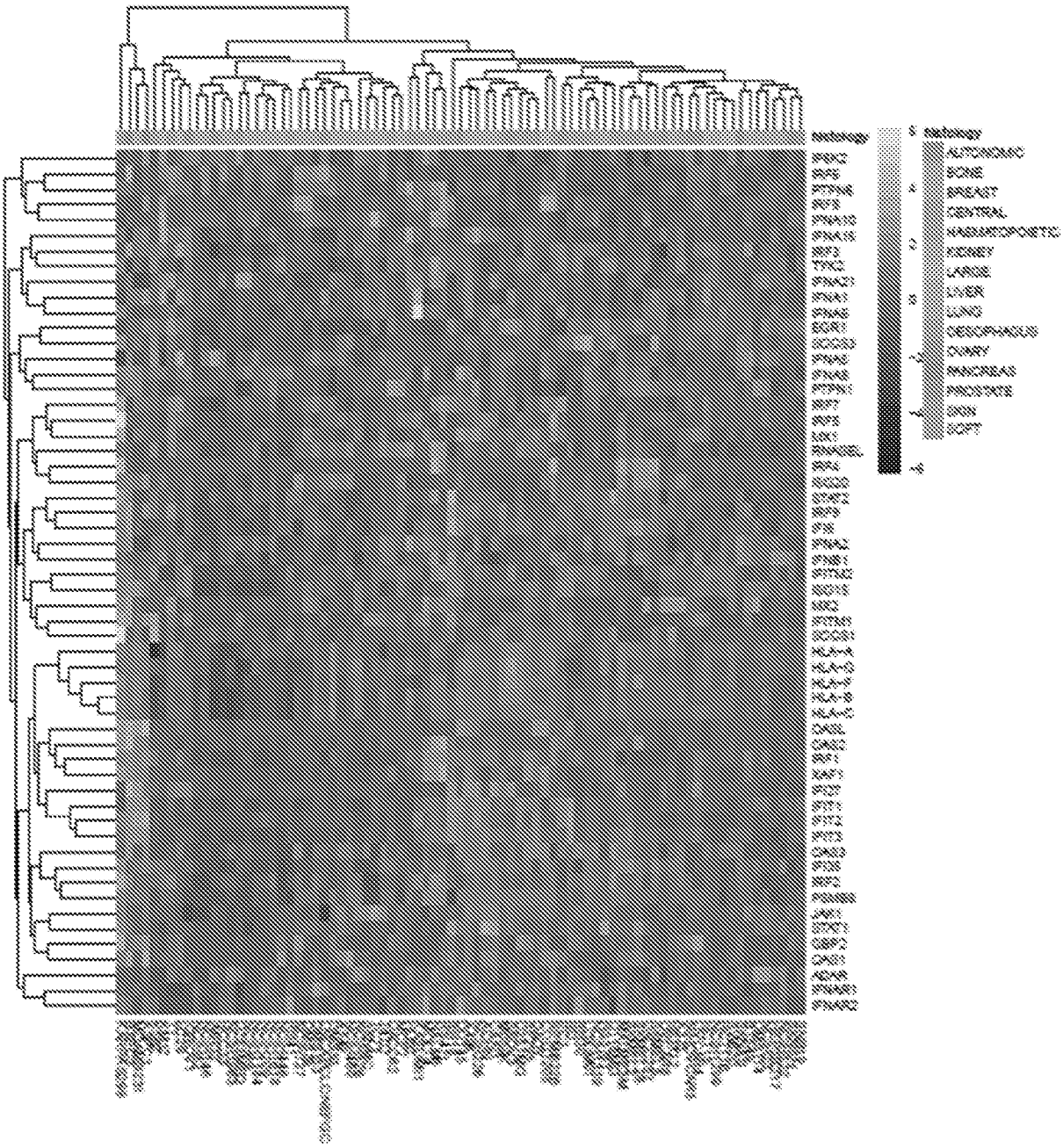


Figure 9

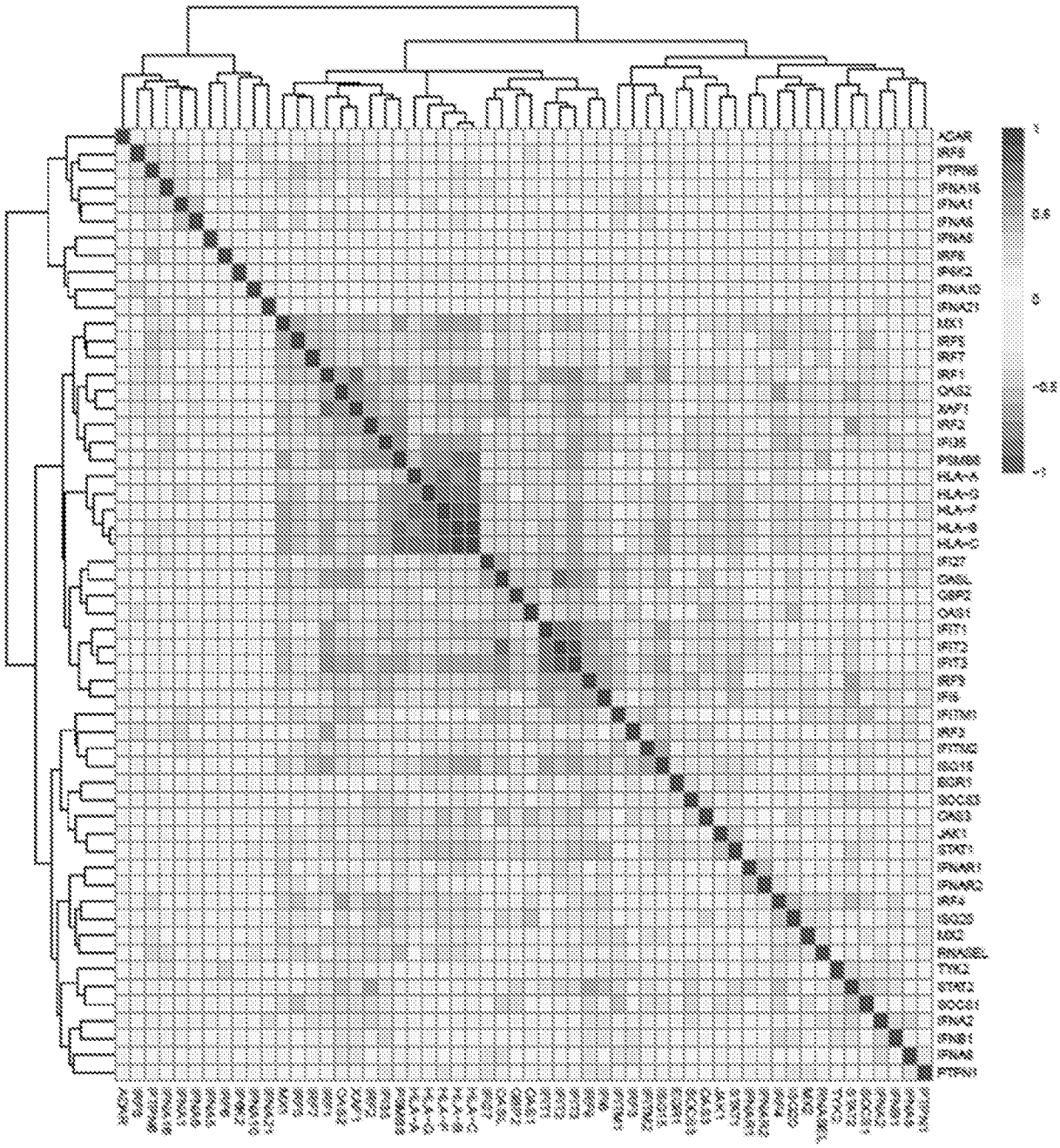


Figure 10

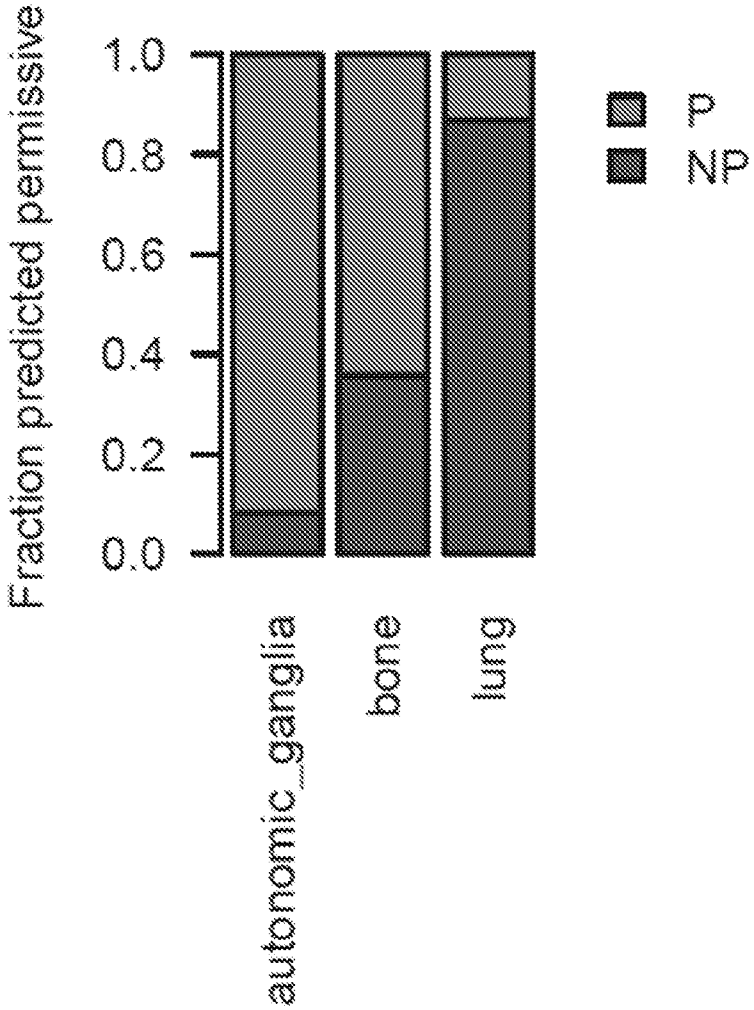

Fraction predicted permissive
1.0
0.8
0.6
0.4
0.2
0.0
P
NP
autonomic_ganglia
bone
lung

Figure 11

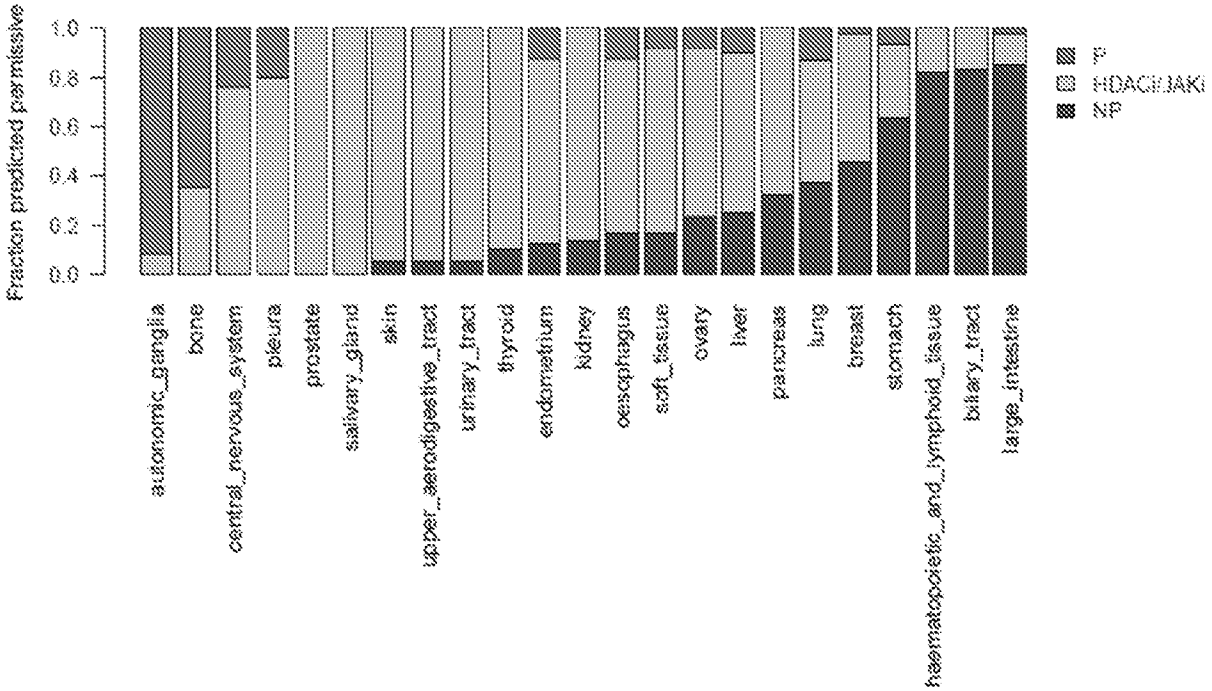

Fraction predicted permissive
1.0
0.8
0.6
0.4
0.2
0.0
P
HDACi/JAKi
NP
autonomic_ganglia
bone
central_nervous_system
pleura
prostate
salivary_gland
skin
upper_aerodigestive_tract
urinary_tract
thyroid
endometrium
kidney
oesophagus
soft_tissue
ovary
liver
pancreas
lung
breast
stomach
haematopoietic_and_lymphoid_tissue
biliary_tract
large_intestine

Figure 12

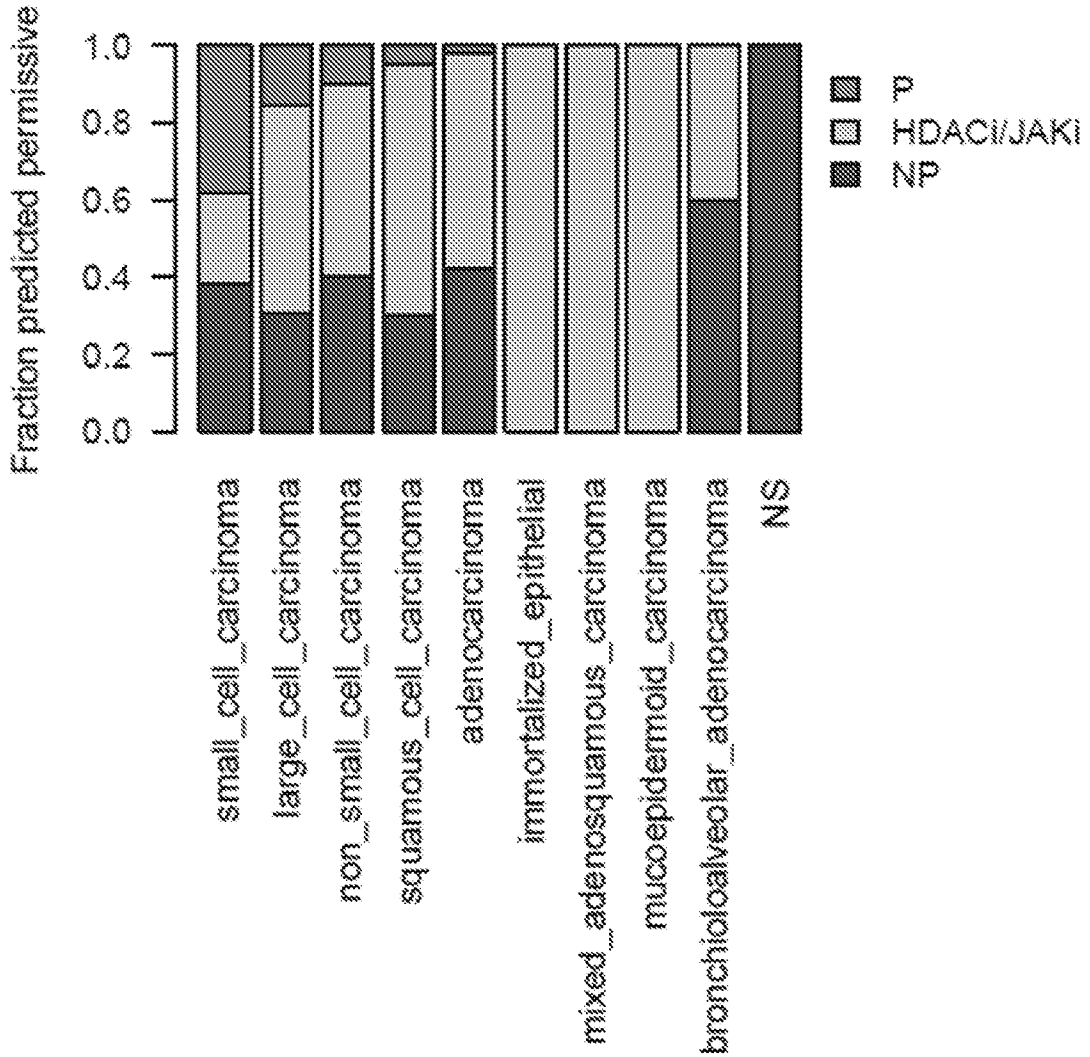

Fraction predicted permissive
0.0
0.2
0.4
0.6
0.8
1.0
P
HDACi/JAKi
NP
small_cell_carcinoma
large_cell_carcinoma
non_small_cell_carcinoma
squamous_cell_carcinoma
adenocarcinoma
immortalized_epithelial
mixed_adenosquamous_carcinoma
mucoepidermoid_carcinoma
bronchioloalveolar_adenocarcinoma
NS

Figure 13

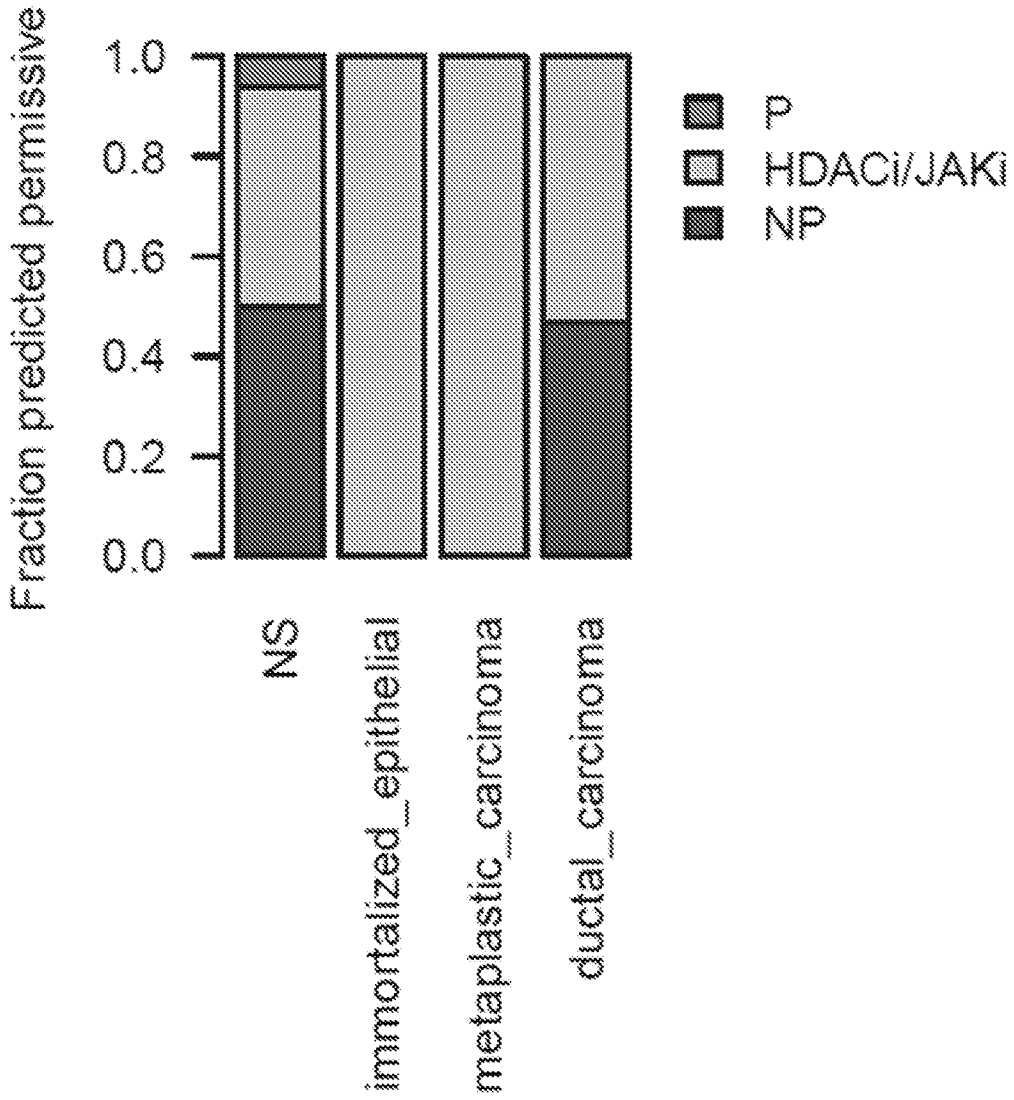

Fraction predicted permissive
1.0
0.8
0.6
0.4
0.2
0.0
NS
immortalized_epithelial
metaplastic_carcinoma
ductal_carcinoma
P
HDACi/JAKi
NP

Figure 14

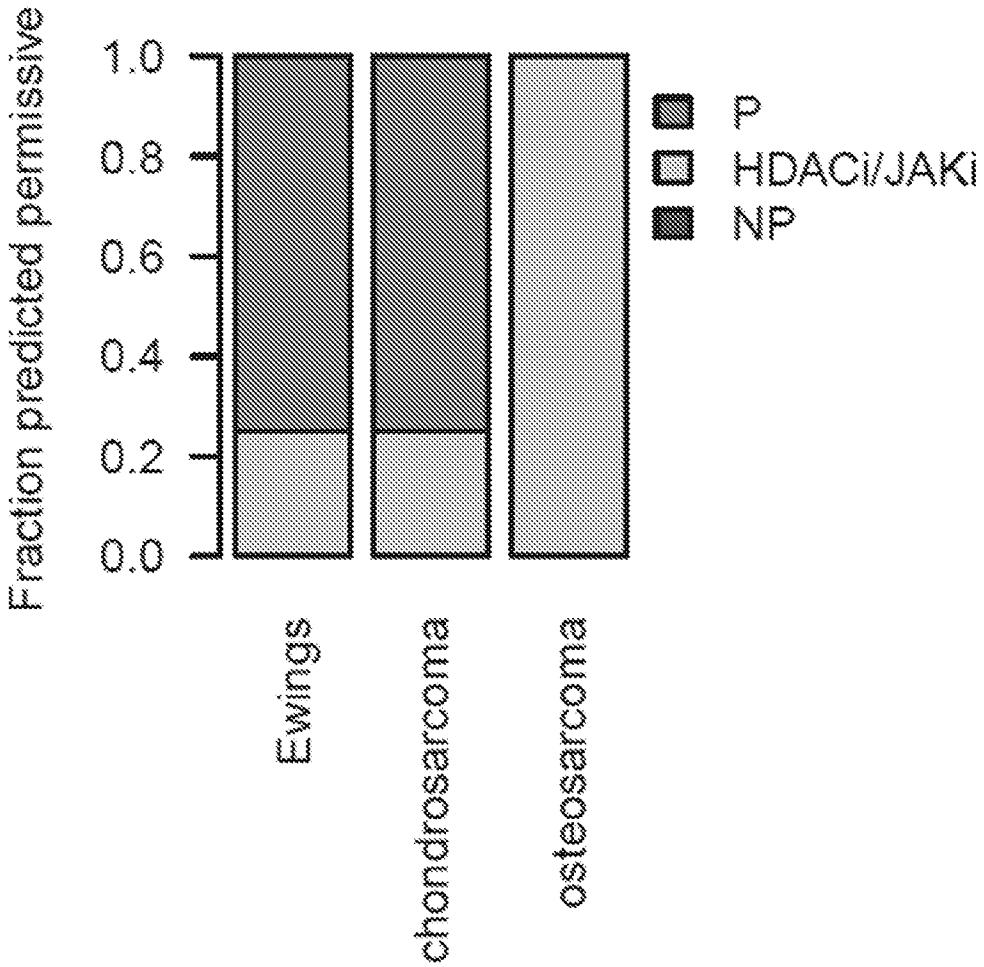

Fraction predicted permissive
1.0
0.8
0.6
0.4
0.2
0.0
P
HDACi/JAKi
NP
Ewings
chondrosarcoma
osteosarcoma

Figure 15

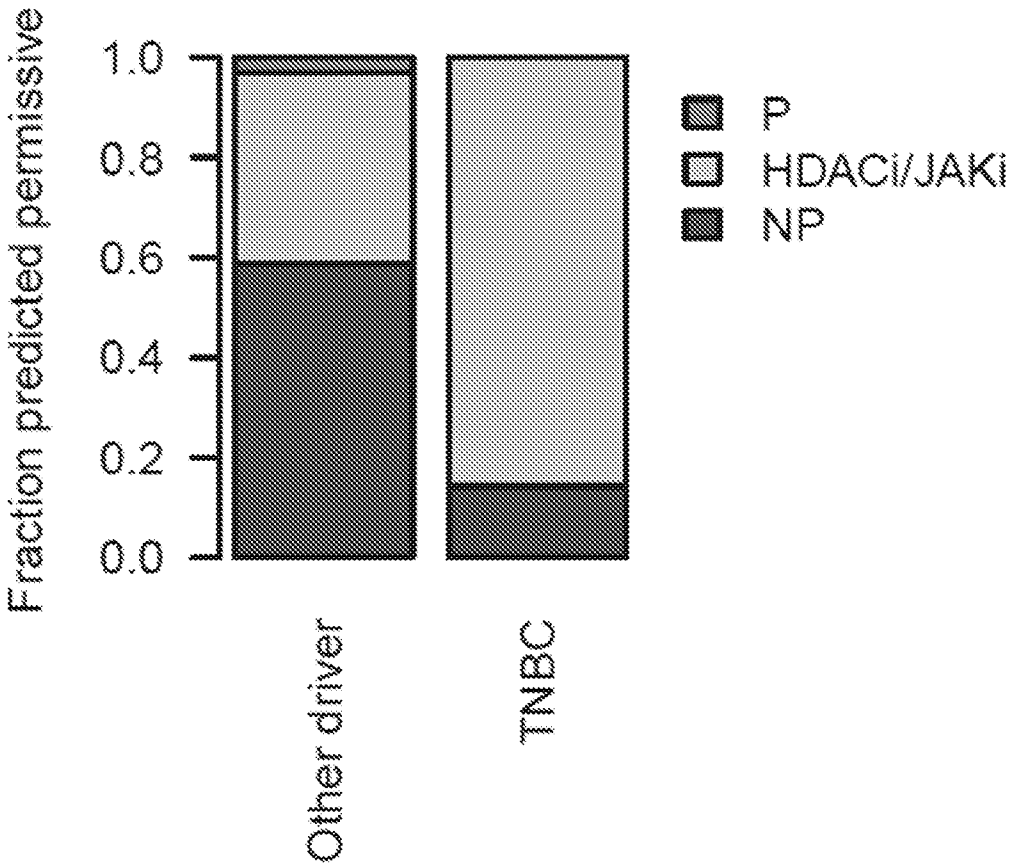

Fraction predicted permissive
1.0
0.8
0.6
0.4
0.2
0.0
Other driver
TNBC
P
HDACi/JAKi
NP

Figure 16

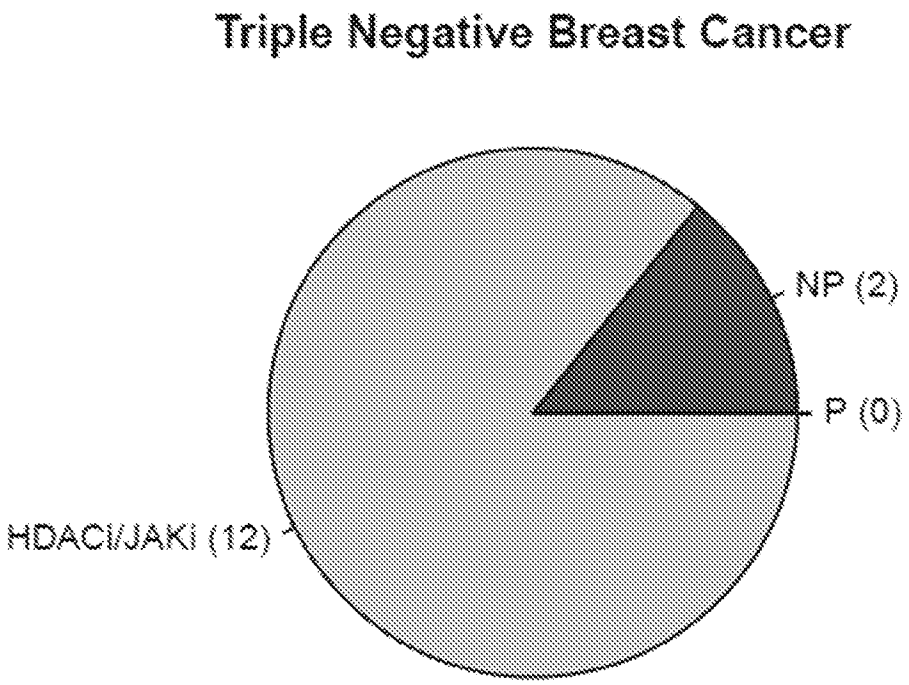


Figure 17

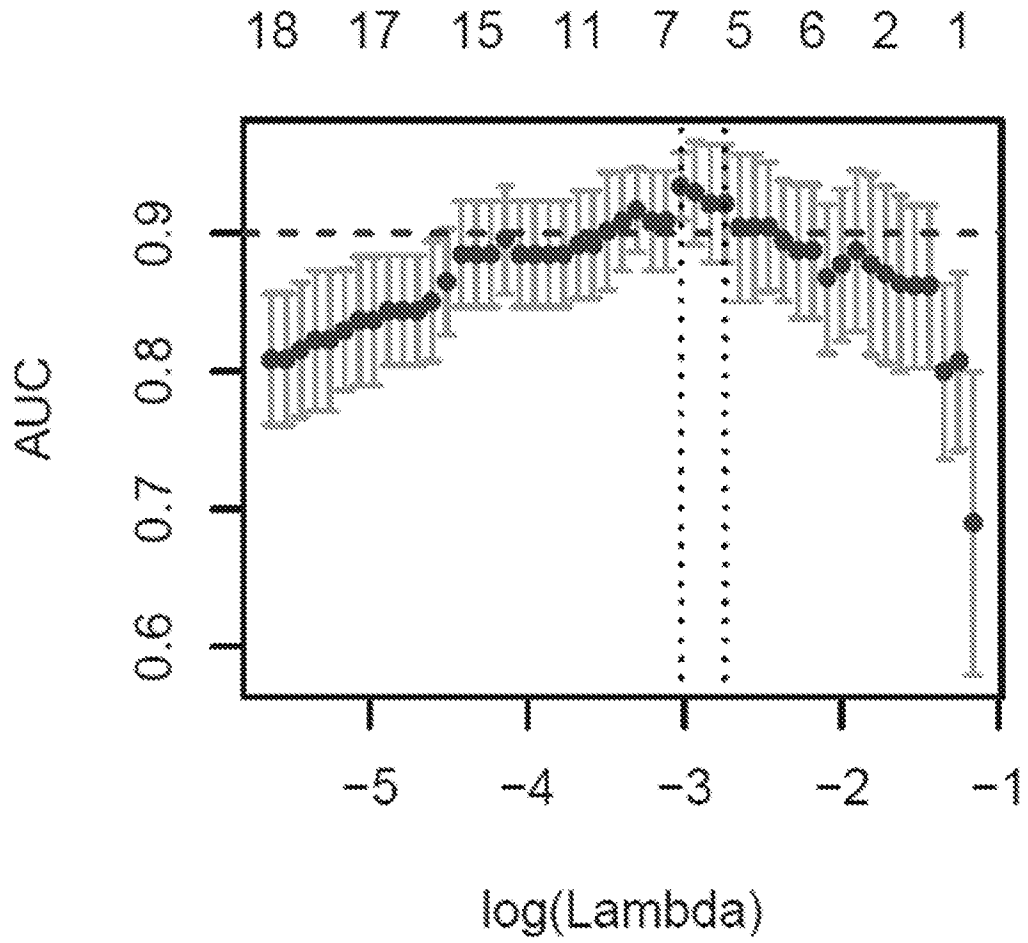


Figure 18

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
A101D	skin	malignant_melanoma	NP	P	NP
A1207	central_nervous_system	glioma	NP	P	NP
A172	central_nervous_system	glioma	NP	P	NP
A204	soft_tissue	rhabdoid_tumour	NP	P	NP
A2058	skin	malignant_melanoma	NP	P	NP
A253	salivary_gland	carcinoma	NP	P	NP
A2780	ovary	carcinoma	NP	P	NP
A673	bone	Ewings_sarcoma	NP	P	NP
A704	kidney	carcinoma	NP	NP	NP
ABC1	lung	carcinoma	P	P	P
ACCMESO1	pleura	mesothelioma	NP	P	NP
AGS	stomach	carcinoma	NP	NP	NP
ALLSIL	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
AM38	central_nervous_system	glioma	NP	P	NP
AML193	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
AMO1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
AU565	breast	carcinoma	NP	NP	NP
AZ521	stomach	carcinoma	NP	NP	NP
BC3C	urinary_tract	carcinoma	NP	P	NP
BCP1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
BCPAP	thyroid	carcinoma	NP	P	NP
BDCM	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
BEN	lung	carcinoma	NP	NP	NP
BFTC905	urinary_tract	carcinoma	NP	P	NP
BFTC909	kidney	carcinoma	NP	P	NP
BHT101	thyroid	carcinoma	NP	P	NP
BHY	upper_aerodigestive_tract	carcinoma	NP	P	NP
BL41	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
BL70	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
BT20	breast	carcinoma	NP	P	NP
BT474	breast	carcinoma	NP	P	NP
BT483	breast	carcinoma	NP	NP	NP
BV173	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
C32	skin	malignant_melanoma	NP	P	NP
C3A	liver	carcinoma	NP	P	NP
CA46	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP

Figure 19

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
CADOES1	bone	Ewings_sarcoma	P	P	P
CAL120	breast	carcinoma	NP	P	NP
CAL12T	lung	carcinoma	NP	P	NP
CAL148	breast	carcinoma	P	NP	NP
CAL29	urinary_tract	carcinoma	NP	P	NP
CAL33	upper_aerodigestive_tract	carcinoma	NP	NP	NP
CAL51	breast	carcinoma	P	P	P
CAL54	kidney	carcinoma	NP	P	NP
CAL62	thyroid	carcinoma	NP	P	NP
CAL78	bone	chondrosarcoma	NP	P	NP
CAL851	breast	carcinoma	NP	P	NP
CAMA1	breast	carcinoma	NP	P	NP
CAS1	central_nervous_system	glioma	NP	P	NP
CCFSTTG1	central_nervous_system	glioma	NP	P	NP
CCK81	large_intestine	carcinoma	NP	NP	NP
CFPAC1	pancreas	carcinoma	NP	NP	NP
CGTHW1	thyroid	carcinoma	NP	P	NP
CH157MN	central_nervous_system	meningioma	NP	P	NP
CHL1	skin	malignant_melanoma	NP	P	NP
CHP126	autonomic_ganglia	neuroblastoma	P	P	P
CHP212	autonomic_ganglia	neuroblastoma	NP	P	NP
CI1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
CJM	skin	malignant_melanoma	NP	P	NP
CL11	large_intestine	carcinoma	NP	NP	NP
CL14	large_intestine	carcinoma	NP	NP	NP
CL34	large_intestine	carcinoma	NP	NP	NP
CL40	large_intestine	carcinoma	NP	NP	NP
CMK115	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
CMK86	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
CMK	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
CMLT1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	P	NP
COLO320	large_intestine	carcinoma	NP	P	NP
COLO677	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
COLO678	large_intestine	carcinoma	NP	NP	NP
COLO679	skin	malignant_melanoma	NP	NP	NP
COLO680N	oesophagus	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
COLO704	ovary	carcinoma	P	P	P
COLO783	skin	malignant_melanoma	NP	P	NP
COLO800	skin	malignant_melanoma	NP	P	NP
COLO818	skin	malignant_melanoma	NP	P	NP
COLO849	skin	malignant_melanoma	NP	P	NP
CORL105	lung	carcinoma	NP	P	NP
CORL23	lung	carcinoma	NP	NP	NP
CORL24	lung	carcinoma	P	P	P
CORL279	lung	carcinoma	P	NP	NP
CORL311	lung	carcinoma	P	NP	NP
CORL47	lung	carcinoma	NP	NP	NP
CORL51	lung	carcinoma	P	NP	NP
CORL88	lung	carcinoma	P	NP	NP
CORL95	lung	carcinoma	NP	P	NP
COV318	ovary	carcinoma	NP	P	NP
COV362	ovary	carcinoma	NP	P	NP
COV434	ovary	sex_cord-stromal_tumour	NP	NP	NP
COV504	ovary	carcinoma	NP	P	NP
COV644	ovary	carcinoma	NP	P	NP
CPCN	lung	carcinoma	NP	NP	NP
CW2	large_intestine	carcinoma	NP	NP	NP
DANG	pancreas	carcinoma	NP	P	NP
DB	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
DBTRG05MG	central_nervous_system	glioma	NP	P	NP
DEL	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
DFCI024	lung	carcinoma	NP	P	NP
DKMG	central_nervous_system	glioma	NP	P	NP
DLD1	large_intestine	carcinoma	NP	NP	NP
DM3	pleura	mesothelioma	NP	P	NP
DND41	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
DOHH2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
DU4475	breast	carcinoma	P	NP	NP
DV90	lung	carcinoma	NP	NP	NP
EB1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
EB2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
EBC1	lung	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
ECC10	stomach	carcinoma	P	NP	NP
ECC12	stomach	carcinoma	NP	NP	NP
ECGI10	oesophagus	carcinoma	NP	P	NP
EFE184	endometrium	carcinoma	NP	P	NP
EFM192A	breast	carcinoma	NP	NP	NP
EFM19	breast	carcinoma	NP	P	NP
EFO21	ovary	carcinoma	NP	P	NP
EFO27	ovary	carcinoma	NP	P	NP
EHEB	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
EJM	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
EM2	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
EN	endometrium	carcinoma	P	P	P
EOL1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
EPLC272H	lung	carcinoma	NP	P	NP
ES2	ovary	carcinoma	NP	P	NP
ESS1	endometrium	carcinoma	NP	P	NP
EVSAT	breast	carcinoma	P	NP	NP
EW8	bone	Ewings_sarcoma	NP	P	NP
EWS502	bone	Ewings_sarcoma	P	P	P
F36P	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
F5	central_nervous_system	meningioma	NP	P	NP
FTC133	thyroid	carcinoma	NP	P	NP
FTC238	thyroid	carcinoma	NP	P	NP
FU97	stomach	carcinoma	NP	NP	NP
FUOV1	ovary	carcinoma	NP	P	NP
G361	skin	malignant_melanoma	NP	P	NP
G401	soft_tissue	rhabdoid_tumour	NP	P	NP
G402	soft_tissue	rhabdoid_tumour	NP	NP	NP
GA10	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
GAMG	central_nervous_system	glioma	NP	P	NP
GB1	central_nervous_system	glioma	NP	P	NP
GCIY	stomach	carcinoma	NP	P	NP
GCT	soft_tissue	malignant_fibrous_sarcoma	NP	P	NP
GDM1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
GI1	central_nervous_system	glioma	NP	P	NP
GMS10	central_nervous_system	glioma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
GOS3	central_nervous_system	glioma	NP	P	NP
GRANTA519	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
GRM	skin	malignant_melanoma	NP	P	NP
GSS	stomach	carcinoma	NP	NP	NP
GSU	stomach	carcinoma	NP	NP	NP
H4	central_nervous_system	glioma	NP	P	NP
HARA	lung	carcinoma	NP	P	NP
HCC1143	breast	carcinoma	NP	P	NP
HCC1171	lung	carcinoma	NP	P	NP
HCC1187	breast	carcinoma	NP	P	NP
HCC1195	lung	carcinoma	NP	P	NP
HCC1359	lung	carcinoma	NP	P	NP
HCC1395	breast	carcinoma	NP	P	NP
HCC1419	breast	carcinoma	NP	NP	NP
HCC1428	breast	carcinoma	NP	NP	NP
HCC1438	lung	carcinoma	NP	P	NP
HCC1500	breast	carcinoma	NP	NP	NP
HCC1569	breast	carcinoma	NP	P	NP
HCC1588	lung	carcinoma	NP	NP	NP
HCC1599	breast	carcinoma	NP	P	NP
HCC15	lung	carcinoma	NP	P	NP
HCC1806	breast	carcinoma	NP	P	NP
HCC1833	lung	carcinoma	P	NP	NP
HCC1897	lung	carcinoma	NP	NP	NP
HCC1937	breast	carcinoma	NP	P	NP
HCC1954	breast	carcinoma	NP	P	NP
HCC202	breast	carcinoma	NP	NP	NP
HCC2108	lung	carcinoma	NP	P	NP
HCC2157	breast	carcinoma	P	P	P
HCC2218	breast	carcinoma	NP	NP	NP
HCC2279	lung	carcinoma	NP	P	NP
HCC2814	lung	carcinoma	NP	P	NP
HCC2935	lung	carcinoma	NP	NP	NP
HCC364	lung	carcinoma	NP	NP	NP
HCC366	lung	carcinoma	NP	P	NP
HCC38	breast	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
HCC4006	lung	carcinoma	NP	P	NP
HCC44	lung	carcinoma	NP	P	NP
HCC56	large_intestine	carcinoma	NP	NP	NP
HCC70	breast	carcinoma	NP	P	NP
HCC78	lung	carcinoma	NP	NP	NP
HCC827GR5	lung	carcinoma	NP	NP	NP
HCC827	lung	carcinoma	NP	NP	NP
HCC95	lung	carcinoma	NP	P	NP
HCT8	large_intestine	carcinoma	NP	NP	NP
HDLM2	Haematopoietic_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
HDMYZ	haematopoietic_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
HDQP1	breast	carcinoma	NP	P	NP
HEC108	endometrium	carcinoma	NP	NP	NP
HEC151	endometrium	carcinoma	NP	P	NP
HEC1A	endometrium	carcinoma	NP	P	NP
HEC1B	endometrium	carcinoma	NP	P	NP
HEC251	endometrium	carcinoma	NP	P	NP
HEC265	endometrium	carcinoma	P	P	P
HEC50B	endometrium	carcinoma	NP	NP	NP
HEC59	endometrium	carcinoma	NP	NP	NP
HEC6	endometrium	carcinoma	NP	P	NP
HEL	haematopoietic_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
HGC27	stomach	carcinoma	NP	P	NP
HH	haematopoietic _lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
HK2	kidney	other	NP	P	NP
HLC1	lung	carcinoma	NP	P	NP
HLE	liver	carcinoma	NP	P	NP
HLF	liver	carcinoma	NP	P	NP
HMC18	breast	carcinoma	NP	P	NP
HMCB	skin	malignant_melanoma	NP	P	NP
HMEL	breast	other	NP	P	NP
HOS	bone	osteosarcoma	P	P	P
HPAC	pancreas	carcinoma	P	P	P
HPAFII	pancreas	carcinoma	NP	NP	NP
HPBALL	haematopoietic _lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
HSC2	upper_aerodigestive_tract	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
HSC3	upper_aerodigestive_tract	carcinoma	NP	P	NP
HSC4	upper_aerodigestive_tract	carcinoma	NP	P	NP
HT1080	soft_tissue	fibrosarcoma	NP	P	NP
HT115	large_intestine	carcinoma	NP	NP	NP
HT1197	urinary_tract	carcinoma	NP	NP	NP
HT1376	urinary_tract	carcinoma	NP	P	NP
HT144	skin	malignant_melanoma	NP	P	NP
HT55	large_intestine	carcinoma	NP	NP	NP
HT	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
HTK	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
HUPT3	pancreas	carcinoma	NP	P	NP
HUPT4	pancreas	carcinoma	NP	P	NP
IALM	lung	carcinoma	NP	P	NP
IGR1	skin	malignant_melanoma	NP	P	NP
IGR37	skin	malignant_melanoma	NP	P	NP
IGR39	skin	malignant_melanoma	NP	P	NP
IM95	stomach	carcinoma	NP	NP	NP
IPC298	skin	malignant_melanoma	NP	P	NP
ISTMES1	pleura	mesothelioma	NP	P	NP
ISTMES2	pleura	mesothelioma	NP	P	NP
J82	urinary_tract	carcinoma	NP	P	NP
JHH1	liver	carcinoma	NP	NP	NP
JHH2	liver	carcinoma	NP	NP	NP
JHH4	liver	carcinoma	NP	P	NP
JHH5	liver	carcinoma	NP	NP	NP
JHH6	liver	carcinoma	NP	P	NP
JHH7	liver	carcinoma	NP	NP	NP
JHOC5	ovary	carcinoma	NP	P	NP
JHOM1	ovary	carcinoma	NP	P	NP
JHOM2B	ovary	carcinoma	NP	NP	NP
JHOS2	ovary	carcinoma	NP	P	NP
JHOS4	ovary	carcinoma	NP	NP	NP
JHUEM1	endometrium	carcinoma	NP	P	NP
JHUEM2	endometrium	carcinoma	P	P	P
JHUEM3	endometrium	carcinoma	NP	P	NP
JIMT1	breast	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
JJN3	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
JK1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
JL1	pleura	mesothelioma	NP	P	NP
JM1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
JMSU1	urinary_tract	carcinoma	NP	P	NP
JURKAT	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
JURLMK1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
JVM2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
JVM3	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
K029AX	skin	malignant_melanoma	NP	P	NP
KALS1	central_nervous_system	glioma	NP	P	NP
KARPAS422	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KARPAS620	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KASUMI2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KCIMOH1	pancreas	carcinoma	NP	P	NP
KCL22	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	P	NP
KE37	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
KE39	stomach	carcinoma	NP	NP	NP
KE97	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KELLY	autonomic_ganglia	neuroblastoma	P	P	P
KG1C	central_nervous_system	glioma	NP	P	NP
KG1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
KHM1B	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KLE	endometrium	carcinoma	NP	P	NP
KLM1	pancreas	carcinoma	NP	P	NP
KMBC2	urinary_tract	carcinoma	NP	P	NP
KMH2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KMM1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
KMRC1	kidney	carcinoma	NP	P	NP
KMRC20	kidney	carcinoma	NP	NP	NP
KMRC2	kidney	carcinoma	NP	P	NP
KMRC3	kidney	carcinoma	NP	P	NP
KMS11	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KMS12BM	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KMS18	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KMS20	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
KMS21BM	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KMS26	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KMS27	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KMS28BM	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
KMS34	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
KNS42	central_nervous_system	glioma	NP	P	NP
KNS60	central_nervous_system	glioma	NP	P	NP
KNS62	lung	carcinoma	NP	P	NP
KNS81	central_nervous_system	glioma	NP	P	NP
KO52	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
KOPN8	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
KP2	pancreas	carcinoma	NP	P	NP
KP3	pancreas	carcinoma	NP	NP	NP
KP4	pancreas	carcinoma	NP	P	NP
KPL1	breast	carcinoma	NP	NP	NP
KPNRTBM1	autonomic_ganglia	neuroblastoma	P	P	P
KPNYN	autonomic_ganglia	neuroblastoma	P	P	P
KS1	central_nervous_system	glioma	NP	P	NP
KU1919	urinary_tract	carcinoma	P	P	P
KU812	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
KURAMOCHI	ovary	carcinoma	NP	P	NP
KYM1	soft_tissue	rhabdomyosarcoma	NP	NP	NP
KYO1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	P	NP
KYSE140	oesophagus	carcinoma	P	P	P
KYSE150	oesophagus	carcinoma	NP	P	NP
KYSE180	oesophagus	carcinoma	NP	P	NP
KYSE270	oesophagus	carcinoma	NP	P	NP
KYSE30	oesophagus	carcinoma	NP	P	NP
KYSE410	oesophagus	carcinoma	NP	P	NP
KYSE450	oesophagus	carcinoma	NP	P	NP
KYSE510	oesophagus	carcinoma	NP	P	NP
KYSE520	oesophagus	carcinoma	NP	P	NP
KYSE70	oesophagus	carcinoma	NP	P	NP
L1236	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
L363	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
L428	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
L540	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
LAMA84	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
LC1F	lung	carcinoma	NP	P	NP
LCLC103H	lung	carcinoma	NP	P	NP
LCLC97TM1	lung	carcinoma	NP	NP	NP
LK2	lung	carcinoma	P	P	P
LMSU	stomach	carcinoma	NP	P	NP
LN18	central_nervous_system	glioma	NP	P	NP
LN215	central_nervous_system	glioma	NP	P	NP
LN229	central_nervous_system	glioma	NP	P	NP
LN235	central_nervous_system	glioma	NP	P	NP
LN319	central_nervous_system	glioma	NP	P	NP
LN340	central_nervous_system	glioma	NP	P	NP
LN382	central_nervous_system	glioma	NP	P	NP
LN428	central_nervous_system	glioma	NP	P	NP
LN443	central_nervous_system	glioma	NP	P	NP
LN464	central_nervous_system	glioma	NP	P	NP
LNZ308	central_nervous_system	glioma	NP	P	NP
LOUNH91	lung	carcinoma	NP	P	NP
LP1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
LS1034	large_intestine	carcinoma	NP	NP	NP
LS123	large_intestine	carcinoma	NP	P	NP
LS411N	large_intestine	carcinoma	NP	NP	NP
LS513	large_intestine	carcinoma	NP	NP	NP
LU65	lung	carcinoma	P	NP	NP
LU99	lung	carcinoma	NP	P	NP
LUDLU1	lung	carcinoma	NP	NP	NP
LXF289	lung	carcinoma	NP	P	NP
MC116	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MCAS	ovary	carcinoma	NP	P	NP
MDAMB134VI	breast	carcinoma	NP	NP	NP
MDAMB157	breast	carcinoma	NP	P	NP
MDAMB175VII	breast	carcinoma	NP	NP	NP
MDAMB361	breast	carcinoma	NP	P	NP
MDAMB415	breast	carcinoma	NP	NP	NP
MDAMB435S	skin	malignant_melanoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
MDAMB436	breast	carcinoma	NP	P	NP
MDAMB453	breast	carcinoma	P	NP	NP
MDAMB468	breast	carcinoma	NP	P	NP
MDST8	large_intestine	carcinoma	NP	P	NP
ME1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
MEC1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MEC2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MEG01	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
MELHO	skin	malignant_melanoma	NP	P	NP
MELJUSO	skin	malignant_melanoma	NP	P	NP
MESSA	soft_tissue	sarcoma	NP	P	NP
MFE280	endometrium	carcinoma	NP	P	NP
MFE296	endometrium	carcinoma	NP	P	NP
MFE319	endometrium	carcinoma	NP	P	NP
MG63	bone	osteosarcoma	NP	P	NP
MHHCALL2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MHHCALL3	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MHHCALL4	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MHHES1	bone	Ewings_sarcoma	NP	P	NP
MHHNB11	autonomic_ganglia	neuroblastoma	P	P	P
MJ	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MKN1	stomach	carcinoma	NP	P	NP
MKN45	stomach	carcinoma	NP	NP	NP
MKN74	stomach	carcinoma	NP	NP	NP
MKN7	stomach	carcinoma	NP	P	NP
ML1	thyroid	carcinoma	NP	P	NP
MM1S	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MOGGCCM	central_nervous_system	glioma	NP	P	NP
MOGGUVW	central_nervous_system	glioma	NP	P	NP
MOLM13	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
MOLM16	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
MOLM6	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
MOLP2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MOLP8	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
MOLT13	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
MOLT16	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
MONOMAC1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
MONOMAC6	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
MOTN1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MSTO211H	pleura	mesothelioma	NP	P	NP
MUTZ5	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
MV411	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
NALM19	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
NALM1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
NAMALWA	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
NB1	autonomic_ganglia	neuroblastoma	P	P	P
NB4	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
NCIH1048	lung	carcinoma	NP	P	NP
NCIH1092	lung	carcinoma	P	P	P
NCIH1105	lung	carcinoma	P	P	P
NCIH1155	lung	carcinoma	NP	P	NP
NCIH1341	lung	carcinoma	P	P	P
NCIH1355	lung	carcinoma	NP	P	NP
NCIH1373	lung	carcinoma	NP	P	NP
NCIH1385	lung	carcinoma	NP	NP	NP
NCIH1395	lung	carcinoma	NP	NP	NP
NCIH1435	lung	carcinoma	NP	NP	NP
NCIH1436	lung	carcinoma	P	P	P
NCIH1437	lung	carcinoma	NP	NP	NP
NCIH1563	lung	carcinoma	NP	P	NP
NCIH1568	lung	carcinoma	NP	P	NP
NCIH1573	lung	carcinoma	NP	NP	NP
NCIH1581	lung	carcinoma	NP	NP	NP
NCIH1623	lung	carcinoma	NP	P	NP
NCIH1648	lung	carcinoma	NP	P	NP
NCIH1650	lung	carcinoma	NP	P	NP
NCIH1651	lung	carcinoma	NP	P	NP
NCIH1666	lung	carcinoma	NP	P	NP
NCIH1693	lung	carcinoma	NP	P	NP
NCIH1694	lung	carcinoma	P	P	P
NCIH1703	lung	carcinoma	NP	P	NP
NCIH1734	lung	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
NCIH1755	lung	carcinoma	NP	P	NP
NCIH1781	lung	carcinoma	NP	NP	NP
NCIH1792	lung	carcinoma	NP	P	NP
NCIH1793	lung	carcinoma	NP	P	NP
NCIH1836	lung	carcinoma	NP	NP	NP
NCIH1838	lung	carcinoma	NP	NP	NP
NCIH1869	lung	carcinoma	NP	NP	NP
NCIH1876	lung	carcinoma	P	P	P
NCIH1915	lung	carcinoma	NP	P	NP
NCIH1930	lung	carcinoma	P	P	P
NCIH1944	lung	carcinoma	NP	NP	NP
NCIH196	lung	carcinoma	NP	P	NP
NCIH1975	lung	carcinoma	NP	NP	NP
NCIH2009	lung	carcinoma	NP	P	NP
NCIH2023	lung	carcinoma	NP	P	NP
NCIH2029	lung	carcinoma	NP	P	NP
NCIH2030	lung	carcinoma	NP	P	NP
NCIH2052	pleura	mesothelioma	NP	P	NP
NCIH2066	lung	carcinoma	P	NP	NP
NCIH2081	lung	carcinoma	NP	NP	NP
NCIH2085	lung	carcinoma	P	P	P
NCIH2087	lung	carcinoma	NP	NP	NP
NCIH2106	lung	carcinoma	P	P	P
NCIH2110	lung	carcinoma	NP	NP	NP
NCIH211	lung	carcinoma	P	NP	NP
NCIH2122	lung	carcinoma	NP	NP	NP
NCIH2126	lung	carcinoma	NP	NP	NP
NCIH2141	lung	carcinoma	P	P	P
NCIH2170	lung	carcinoma	NP	NP	NP
NCIH2171	lung	carcinoma	P	P	P
NCIH2172	lung	carcinoma	NP	P	NP
NCIH2196	lung	carcinoma	NP	P	NP
NCIH2227	lung	carcinoma	NP	P	NP
NCIH2228	lung	carcinoma	NP	P	NP
NCIH2286	lung	carcinoma	NP	P	NP
NCIH2291	lung	carcinoma	NP	NP	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
NCIH2342	lung	carcinoma	P	P	P
NCIH2347	lung	carcinoma	NP	NP	NP
NCIH2405	lung	carcinoma	NP	NP	NP
NCIH2444	lung	carcinoma	NP	P	NP
NCIH2452	pleura	mesothelioma	NP	P	NP
NCIH28	pleura	mesothelioma	NP	P	NP
NCIH292	lung	carcinoma	NP	P	NP
NCIH322	lung	carcinoma	P	NP	NP
NCIH3255	lung	carcinoma	NP	P	NP
NCIH358	lung	carcinoma	NP	NP	NP
NCIH441	lung	carcinoma	NP	NP	NP
NCIH508	large_intestine	carcinoma	NP	NP	NP
NCIH510	lung	carcinoma	P	P	P
NCIH520	lung	carcinoma	NP	P	NP
NCIH524	lung	carcinoma	P	P	P
NCIH596	lung	carcinoma	NP	P	NP
NCIH647	lung	carcinoma	NP	P	NP
NCIH650	lung	carcinoma	NP	NP	NP
NCIH660	prostate	carcinoma	NP	P	NP
NCIH661	lung	carcinoma	NP	P	NP
NCIH684	liver	other	NP	NP	NP
NCIH716	large_intestine	carcinoma	NP	NP	NP
NCIH747	large_intestine	carcinoma	NP	NP	NP
NCIH810	lung	carcinoma	P	NP	NP
NCIH838	lung	carcinoma	NP	P	NP
NCIH841	lung	carcinoma	NP	NP	NP
NCIH854	lung	carcinoma	NP	NP	NP
NCIH889	lung	carcinoma	NP	NP	NP
NCIH929	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
NCIN87	stomach	carcinoma	NP	P	NP
NCO2	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
NH6	autonomic_ganglia	neuroblastoma	P	P	P
NMCG1	central_nervous_system	glioma	NP	P	NP
NOMO1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
NUDHL1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
NUDUL1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
NUGC2	stomach	carcinoma	NP	P	NP
NUGC3	stomach	carcinoma	NP	NP	NP
NUGC4	stomach	carcinoma	NP	NP	NP
OAW28	ovary	carcinoma	NP	P	NP
OAW42	ovary	carcinoma	NP	NP	NP
OCIAML2	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
OCIAML3	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
OCIAML5	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
OCILY10	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
OCILY19	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
OCILY3	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
OCIM1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
OCUM1	stomach	carcinoma	NP	NP	NP
OE19	oesophagus	carcinoma	NP	NP	NP
OE33	oesophagus	other	NP	NP	NP
OELE	ovary	other	NP	P	NP
ONCODG1	ovary	carcinoma	P	P	P
ONS76	central_nervous_system	primitive_neuroectodermal	NP	P	NP
OPM2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
OSRC2	kidney	carcinoma	NP	P	NP
OUMS23	large_intestine	carcinoma	P	P	P
OUMS27	bone	chondrosarcoma	P	P	P
OV56	ovary	carcinoma	NP	P	NP
OV7	ovary	carcinoma	NP	P	NP
OV90	ovary	carcinoma	NP	P	NP
OVISE	ovary	carcinoma	NP	NP	NP
OVK18	ovary	carcinoma	NP	NP	NP
OVKATE	ovary	carcinoma	NP	P	NP
OVMANA	ovary	carcinoma	NP	NP	NP
OVSAHO	ovary	carcinoma	NP	P	NP
OVTOKO	ovary	carcinoma	NP	NP	NP
P12ICHIKAWA	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
P3HR1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
PANC1	pancreas	carcinoma	NP	P	NP
PATU8902	pancreas	carcinoma	NP	NP	NP
PATU8988S	pancreas	carcinoma	NP	NP	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
PATU8988T	pancreas	carcinoma	NP	P	NP
PC14	lung	carcinoma	NP	P	NP
PCM6	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
PEER	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
PF382	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
PK1	pancreas	carcinoma	NP	P	NP
PK45H	pancreas	carcinoma	NP	P	NP
PK59	pancreas	carcinoma	NP	NP	NP
PL21	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
PL45	pancreas	carcinoma	NP	P	NP
PSN1	pancreas	carcinoma	NP	P	NP
QGP1	pancreas	carcinoma	NP	P	NP
RCC10RGB	kidney	carcinoma	NP	P	NP
RCC4	kidney	carcinoma	NP	P	NP
RCHACV	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
RCM1	large_intestine	carcinoma	NP	NP	NP
RDES	bone	Ewings_sarcoma	P	P	P
REC1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
RERFGC1B	stomach	carcinoma	NP	P	NP
RERFLCAI	lung	carcinoma	NP	P	NP
RERFLCKJ	lung	carcinoma	NP	NP	NP
RERFLCMS	lung	carcinoma	NP	P	NP
RI1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
RKN	soft_tissue	leiomyosarcoma	NP	P	NP
RKO	large_intestine	carcinoma	NP	NP	NP
RL952	endometrium	carcinoma	NP	P	NP
RL	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
RMGI	ovary	carcinoma	NP	P	NP
RMUGS	ovary	carcinoma	NP	P	NP
RPMI7951	skin	malignant_melanoma	NP	P	NP
RPMI8402	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
RS5	pleura	mesothelioma	NP	P	NP
RT112	urinary_tract	carcinoma	NP	P	NP
RT4	urinary_tract	carcinoma	NP	P	NP
RVH421	skin	malignant_melanoma	NP	P	NP
S117	soft_tissue	sarcoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
SALE	lung	other	NP	P	NP
SBC5	lung	carcinoma	NP	NP	NP
SCC15	upper_aerodigestive_tract	carcinoma	NP	P	NP
SCC25	upper_aerodigestive_tract	carcinoma	NP	P	NP
SCC4	upper_aerodigestive_tract	carcinoma	P	P	P
SCC9	upper_aerodigestive_tract	carcinoma	NP	P	NP
SCLC21H	lung	carcinoma	P	P	P
SEM	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
SF126	central_nervous_system	glioma	NP	P	NP
SF172	central_nervous_system	glioma	NP	P	NP
SF767	central_nervous_system	glioma	NP	P	NP
SH10TC	stomach	carcinoma	NP	P	NP
SH4	skin	malignant_melanoma	NP	P	NP
SHP77	lung	carcinoma	P	P	P
SHSY5Y	autonomic_ganglia	neuroblastoma	P	P	P
SIGM5	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
SIMA	autonomic_ganglia	neuroblastoma	P	P	P
SJRH30	soft_tissue	rhabdomyosarcoma	P	P	P
SJSA1	bone	osteosarcoma	NP	P	NP
SKBR3	breast	carcinoma	NP	NP	NP
SKCO1	large_intestine	carcinoma	NP	NP	NP
SKES1	bone	Ewings_sarcoma	P	P	P
SKHEP1	liver	carcinoma	NP	P	NP
SKLMS1	soft_tissue	sarcoma	NP	P	NP
SKLU1	lung	carcinoma	NP	P	NP
SKM1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
SKMEL1	skin	malignant_melanoma	NP	NP	NP
SKMEL24	skin	malignant_melanoma	NP	P	NP
SKMEL30	skin	malignant_melanoma	NP	P	NP
SKMEL31	skin	malignant_melanoma	NP	P	NP
SKMEL3	skin	malignant_melanoma	NP	P	NP
SKMES1	lung	carcinoma	NP	P	NP
SKMM2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SKNDZ	autonomic_ganglia	neuroblastoma	P	P	P
SKNFI	autonomic_ganglia	neuroblastoma	P	P	P
SKRC20	kidney	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
SKUT1	soft_tissue	leiomyosarcoma	NP	P	NP
SNGM	endometrium	carcinoma	NP	P	NP
SNU1033	large_intestine	carcinoma	NP	NP	NP
SNU1040	large_intestine	carcinoma	NP	NP	NP
SNU1041	upper_aerodigestive_tract	carcinoma	NP	P	NP
SNU1066	upper_aerodigestive_tract	carcinoma	NP	P	NP
SNU1076	upper_aerodigestive_tract	carcinoma	NP	P	NP
SNU1077	endometrium	carcinoma	NP	P	NP
SNU1079	biliary_tract	carcinoma	NP	NP	NP
SNU1105	central_nervous_system	glioma	NP	P	NP
SNU1196	biliary_tract	carcinoma	NP	NP	NP
SNU1197	large_intestine	carcinoma	NP	NP	NP
SNU119	ovary	carcinoma	NP	NP	NP
SNU1214	upper_aerodigestive_tract	carcinoma	NP	P	NP
SNU1272	kidney	carcinoma	NP	P	NP
SNU16	stomach	carcinoma	NP	NP	NP
SNU175	large_intestine	carcinoma	NP	NP	NP
SNU182	liver	carcinoma	P	P	P
SNU1	stomach	carcinoma	P	P	P
SNU201	central_nervous_system	glioma	NP	P	NP
SNU213	pancreas	carcinoma	NP	P	NP
SNU216	stomach	carcinoma	NP	P	NP
SNU245	biliary_tract	carcinoma	NP	NP	NP
SNU283	large_intestine	carcinoma	NP	NP	NP
SNU308	biliary_tract	carcinoma	NP	P	NP
SNU324	pancreas	carcinoma	NP	P	NP
SNU349	kidney	carcinoma	NP	P	NP
SNU387	liver	carcinoma	NP	P	NP
SNU398	liver	carcinoma	NP	P	NP
SNU407	large_intestine	carcinoma	NP	NP	NP
SNU410	pancreas	carcinoma	NP	P	NP
SNU423	liver	carcinoma	NP	P	NP
SNU449	liver	carcinoma	NP	P	NP
SNU466	central_nervous_system	glioma	NP	P	NP
SNU46	upper_aerodigestive_tract	carcinoma	NP	P	NP
SNU475	liver	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
SNU478	biliary_tract	carcinoma	NP	NP	NP
SNU489	central_nervous_system	glioma	NP	P	NP
SNU503	large_intestine	carcinoma	NP	P	NP
SNU520	stomach	carcinoma	NP	NP	NP
SNU5	stomach	carcinoma	NP	NP	NP
SNU601	stomach	carcinoma	NP	NP	NP
SNU61	large_intestine	carcinoma	NP	NP	NP
SNU620	stomach	carcinoma	NP	NP	NP
SNU626	central_nervous_system	glioma	NP	P	NP
SNU668	stomach	carcinoma	NP	P	NP
SNU685	endometrium	carcinoma	P	P	P
SNU719	stomach	carcinoma	NP	NP	NP
SNU738	central_nervous_system	glioma	NP	P	NP
SNU761	liver	carcinoma	NP	P	NP
SNU81	large_intestine	carcinoma	NP	NP	NP
SNU840	ovary	carcinoma	NP	P	NP
SNU869	biliary_tract	carcinoma	NP	NP	NP
SNU878	liver	carcinoma	NP	P	NP
SNU886	liver	carcinoma	NP	P	NP
SNU899	upper_aerodigestive_tract	carcinoma	NP	P	NP
SNU8	ovary	carcinoma	NP	P	NP
SNUC1	large_intestine	carcinoma	NP	NP	NP
SNUC2A	large_intestine	carcinoma	NP	P	NP
SNUC4	large_intestine	carcinoma	NP	NP	NP
SNUC5	large_intestine	carcinoma	NP	NP	NP
SR786	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
ST486	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SUDHL10	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SUDHL1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SUDHL4	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SUDHL5	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SUDHL6	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SUDHL8	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SUIT2	pancreas	carcinoma	NP	NP	NP
SUPB15	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
SUPHD1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
SUPM2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
SUPT11	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
SUPT1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
SW1116	large_intestine	carcinoma	NP	NP	NP
SW1417	large_intestine	carcinoma	NP	NP	NP
SW1463	large_intestine	carcinoma	NP	NP	NP
SW1710	urinary_tract	carcinoma	NP	P	NP
SW403	large_intestine	carcinoma	NP	NP	NP
SW480	large_intestine	carcinoma	NP	P	NP
SW48	large_intestine	carcinoma	NP	NP	NP
SW579	thyroid	carcinoma	NP	P	NP
SW837	large_intestine	carcinoma	NP	NP	NP
SW948	large_intestine	carcinoma	NP	NP	NP
T173	bone	osteosarcoma	NP	P	NP
T24	urinary_tract	carcinoma	NP	P	NP
T3M10	lung	carcinoma	NP	P	NP
T3M4	pancreas	carcinoma	NP	NP	NP
T84	large_intestine	carcinoma	NP	NP	NP
T98G	central_nervous_system	glioma	NP	P	NP
TALL1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	P	NP
TC32	bone	Ewings_sarcoma	NP	P	NP
TCCPAN2	pancreas	carcinoma	NP	NP	NP
TCCSUP	urinary_tract	carcinoma	NP	P	NP
TE10	oesophagus	carcinoma	NP	P	NP
TE11	oesophagus	carcinoma	NP	P	NP
TE14	oesophagus	carcinoma	NP	P	NP
TE15	oesophagus	carcinoma	NP	NP	NP
TE1	oesophagus	carcinoma	NP	P	NP
TE4	oesophagus	carcinoma	P	P	P
TE5	oesophagus	carcinoma	NP	NP	NP
TE6	oesophagus	carcinoma	NP	P	NP
TE8	oesophagus	carcinoma	NP	P	NP
TE9	oesophagus	carcinoma	NP	P	NP
TEN	endometrium	carcinoma	NP	P	NP
TF1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
TGBC11TKB	stomach	carcinoma	NP	NP	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
THP1	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
TM31	central_nervous_system	glioma	NP	P	NP
TOV112D	ovary	carcinoma	NP	P	NP
TOV21G	ovary	carcinoma	NP	P	NP
TT2609C02	thyroid	carcinoma	NP	P	NP
TT	thyroid	carcinoma	NP	NP	NP
TUHR10TKB	kidney	carcinoma	NP	P	NP
TUHR14TKB	kidney	carcinoma	NP	P	NP
TUHR4TKB	kidney	carcinoma	NP	P	NP
U178	central_nervous_system	glioma	NP	P	NP
U266B1	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
U343	central_nervous_system	glioma	NP	P	NP
U937	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
UACC812	breast	carcinoma	NP	NP	NP
UACC893	breast	carcinoma	NP	NP	NP
UBLC1	urinary_tract	carcinoma	NP	P	NP
UMRC2	kidney	carcinoma	NP	P	NP
UMRC6	kidney	carcinoma	NP	P	NP
UMUC1	urinary_tract	carcinoma	NP	P	NP
UMUC3	urinary_tract	carcinoma	NP	P	NP
UOK101	kidney	carcinoma	NP	P	NP
UT7	haematopoietic_and_lymphoid_tissue	haematopoietic_neoplasm	NP	NP	NP
VMCUB1	urinary_tract	carcinoma	NP	P	NP
VMRCLCD	lung	carcinoma	NP	NP	NP
VMRCLCP	lung	carcinoma	NP	P	NP
VMRCRCW	kidney	carcinoma	NP	NP	NP
VMRCRCZ	kidney	carcinoma	NP	P	NP
WM115	skin	malignant_melanoma	NP	P	NP
WM1799	skin	malignant_melanoma	NP	P	NP
WM2664	skin	malignant_melanoma	NP	P	NP
WM793	skin	malignant_melanoma	NP	P	NP
WM88	skin	malignant_melanoma	NP	P	NP
WM983B	skin	malignant_melanoma	NP	P	NP
WSUDLCL2	haematopoietic_and_lymphoid_tissue	lymphoid_neoplasm	NP	NP	NP
YAPC	pancreas	carcinoma	NP	P	NP
YD10B	upper_aerodigestive_tract	carcinoma	NP	P	NP

Figure 19 (cont.)

Cell Line Name	Primary site	Histology	IFN	ANTXR1	Predictor
YD15	salivary_gland	carcinoma	NP	P	NP
YD38	upper_aerodigestive_tract	carcinoma	NP	P	NP
YD8	upper_aerodigestive_tract	carcinoma	NP	P	NP
YH13	central_nervous_system	glioma	NP	P	NP
YKG1	central_nervous_system	glioma	NP	P	NP
YMB1	breast	carcinoma	P	NP	NP
ZR751	breast	carcinoma	NP	NP	NP
ZR7530	breast	carcinoma	NP	NP	NP

Figure 19 (cont.)