WHAT IS CLAIMED IS:

1. A non-replicating virus-derived particle comprising:

an envelope having sufficient number of functional G proteins on the surface of the envelope to allow for the virus-derived particle to bind a surface of a cell and be internalized;

an RNA polynucleotide having a sequence that encodes all the proteins required for new virus particle assembly; and

a mixture of proteins that form a structure around the RNA;

wherein the RNA:

(a) has a sufficiently cross-linked structure such that the RNA sequence, in the cell, cannot be used to:

transcribe the complete genome;

translate all the proteins; or

both;

in order to produce sufficient macromolecules required for new virus particle assembly;

(b) is sufficiently discontinuous such that the RNA sequence, in the cell, cannot be used to:

transcribe the complete genome;

translate all proteins; or

both;

in order to produce sufficient macromolecules required for new virus particle assembly; or

both (a) and (b).

2. The non-replicating virus-derived particle according to claim 1, wherein the functional G protein:

has a sequence that comprises SEQ ID NO: 1;

has a sequence that is at least 75% identical to SEQ ID NO: 1 and that is capable of binding to a surface of a cell and effecting internalization of the particle.

3. The non-replicating virus-derived particle according to claim 1 or 2, wherein the mixture of proteins that form a structure around the RNA comprises at least N, P, M, and L proteins.

4. The non-replicating virus-derived particle according to claim 3, wherein the N protein:

has a sequence that comprises SEQ ID NO: 2; or

has a sequence that is at least 80% identical to SEQ ID NO: 2 and that is capable of participating in the formation of the protein structure.

5. The non-replicating virus-derived particle according to claim 3 or 4, wherein the P protein:

has a sequence that comprises SEQ ID NO: 3; or

has a sequence that is at least 80% identical to SEQ ID NO: 3 and that is capable of participating in the formation of the protein structure.

6. The non-replicating virus-derived particle according to any one of claims 3-5, wherein the M protein:

has a sequence that comprises SEQ ID NO: 4; or

has a sequence that is at least 80% identical to SEQ ID NO: 4 and that is capable of participating in the formation of the protein structure.

7. The non-replicating virus-derived particle according to any one of claims 3-6, wherein the L protein:

has a sequence that comprises SEQ ID NO: 5; or

has a sequence that is at least 70% identical to SEQ ID NO: 5 and that is capable of participating in the formation of the protein structure.

8. The non-replicating virus-derived particle according to any one of claims 3-7, wherein the RNA sequence produces functional N, P, M and G proteins on binding and internalization of the particle, and lacks the ability to produce functional L protein.

9. The non-replicating virus-derived particle according to any one of claims 3-7, wherein the RNA sequence produces N, P and M proteins on binding and internalization of the particle, and lacks the ability to produce functional G and L proteins.

10. The non-replicating virus-derived particle according to any one of claims 3-7, wherein the RNA sequence produces N and P proteins on binding and internalization of the particle, and lacks the ability to produce functional M, G and L proteins.

11. The non-replicating virus-derived particle according to any one of claims 3-7, wherein the RNA sequence produces N protein on binding and internalization of the particle, and lacks the ability to produce functional P, M, G and L proteins.

12. The non-replicating virus-derived particle according to any one of claims 3-7, wherein the RNA sequence lacks the ability to produce functional N, P, M, G and L proteins.

13. The non-replicating virus-derived particle according to any one of claims 1-12, wherein the surface of the envelope has at least 60 functional G proteins per particle.

14. The non-replicating virus-derived particle according to any one of claims 1-12, wherein the surface of the envelope has at least 600 functional G proteins per particle.

15. The non-replicating virus-derived particle according to any one of claims 1-12, wherein the surface of the envelope has at least 1200 functional G proteins per particle.

16. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the cross-linked RNA includes at least 0.05% cross-linked nucleotides.

17. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the cross-linked RNA includes at least 0.5% cross-linked nucleotides.

18. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the cross-linked RNA includes at least 1% cross-linked nucleotides.

19. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the cross-linked RNA includes at least 10% cross-linked nucleotides.

20. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the cross-linked RNA includes at least 20% cross-linked nucleotides.

21. The non-replicating virus-derived particle according to any one of claims 16-20, wherein the cross-linked RNA includes less than 80% cross-linked nucleotides.

22. The non-replicating virus-derived particle according to any one of claims 1-21, wherein the RNA structure is cross-linked to RNA, is cross-linked to a protein in the protein structure around the RNA, or both.

23. The non-replicating virus-derived particle according to any one of claims 1-22, wherein the protein structure around the RNA comprises a protein that is:

cross-linked to another protein of the protein structure;
internally cross-linked;
cross-linked to the RNA structure; or
any combination thereof.

24. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the RNA comprises at least two discontinuous RNA polynucleotides.

25. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the RNA comprises at least five discontinuous RNA polynucleotides.

26. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the RNA comprises at least 10 discontinuous RNA polynucleotides.

27. The non-replicating virus-derived particle according to any one of claims 1-15, wherein the RNA comprises at least 100 discontinuous RNA polynucleotides.

28. The non-replicating virus-derived particle according to any one of claims 1-15 wherein the RNA comprises discontinuous RNA polynucleotides of no more than 1000 nucleotides.

29. The non-replicating virus-derived particle according to any one of claims 1-15 wherein the RNA comprises discontinuous RNA polynucleotides of no more than 3000 nucleotides.

30. The non-replicating virus-derived particle according to any one of claims 1-15 wherein the RNA comprises discontinuous RNA polynucleotides of no more than 5000 nucleotides.

31. The non-replicating virus-derived particle according to any one of claims 1-15 wherein the RNA comprises discontinuous RNA polynucleotides of no more than 7000 nucleotides.

32. The non-replicating virus-derived particle according to any one of claims 1-15 wherein the RNA comprises discontinuous RNA polynucleotides of no more than 10,000 nucleotides.

33. A method of producing a non-replicating virus-derived particle from a live virus comprising RNA having a sequence that encodes N, P, M, G or L proteins, the method comprising:

optionally separating the live virus from a UV-absorbing compound;

subjecting the live virus to an RNA damaging agent to:

(a) sufficiently cross-link the RNA structure of the live virus so that, when the virus-derived particle is in a cell:

RNA transcription into mRNA is reduced;

mRNA translation into protein is reduced; or

both;

thereby preventing production of sufficient proteins required for new virus particle assembly;

(b) sufficiently cleaving the RNA structure of the live virus into discontinuous RNA segments so that, when the virus-derived particle is in a cell:

RNA transcription into mRNA is reduced;

mRNA translation into protein is reduced; or

both;

thereby preventing production of sufficient proteins required for new virus particle assembly; or

(c) both (a) and (b).

34. The method according to claim 33, wherein the G protein:

has a sequence that comprises SEQ ID NO: 1;

has a sequence that is at least 75% identical to SEQ ID NO: 1 and that is capable of binding to a surface of a cell and effecting internalization of the particle.

35. The method according to claim 33 or 34, wherein the N protein:

has a sequence that comprises SEQ ID NO: 2; or

has a sequence that is at least 80% identical to SEQ ID NO: 2 and that is capable of participating in the formation of the protein structure.

36. The method according to any one of claims 33-35, wherein the P protein:

has a sequence that comprises SEQ ID NO: 3; or

has a sequence that is at least 80% identical to SEQ ID NO: 3 and that is capable of participating in the formation of the protein structure.

37. The method according to any one of claims 33-36, wherein the M protein:

has a sequence that comprises SEQ ID NO: 4; or

has a sequence that is at least 80% identical to SEQ ID NO: 4 and that is capable of participating in the formation of the protein structure.

38. The method according to any one of claims 33-37, wherein the L protein:

has a sequence that comprises SEQ ID NO: 5; or

has a sequence that is at least 70% identical to SEQ ID NO: 5 and that is capable of participating in the formation of the protein structure.

39. The method according to any one of claims 33-38, wherein subjecting the live virus to an RNA damaging agent comprises subjecting the live virus to electromagnetic radiation.

40. The method according to claim 39, wherein the electromagnetic radiation has a wavelength less than about 1 mm.

41. The method according to claim 39, wherein the electromagnetic radiation has a wavelength less than about 500 nm.

42. The method according to claim 39, wherein the electromagnetic radiation has a wavelength less than about 280 nm.

43. The method according to claim 39, wherein the electromagnetic radiation has a wavelength between about 1 picometer and about 300 nm.

44. The method according to claim 39, wherein the electromagnetic radiation has a wavelength between about 100 nm and about 400 nm, and wherein the live virus is subjected to a dose of electromagnetic radiation between about 100 mJ/cm^2 and about 8,000 mJ/cm^2.

45. The method according to claim 39, wherein the electromagnetic radiation has a wavelength between about 100 nm and about 400 nm, wherein the live virus is subjected to a dose of electromagnetic radiation between about 100 mJ/cm^2 and about 1000 mJ/cm^2.

46. The method according to claim 39, wherein the electromagnetic radiation has a wavelength between about 100 nm and about 400 nm, wherein the live virus is subjected to a dose of electromagnetic radiation between about 150 mJ/cm^2 and about 500 mJ/cm^2.

47. The method according to claim 39, wherein the electromagnetic radiation has a wavelength between about 100 nm and about 280 nm, and the live virus is subjected to a dose of electromagnetic radiation between about 150 and about 300 mJ/cm^2.

48. The method according to claim 39, wherein the electromagnetic radiation is gamma irradiation, and the live virus is subjected to a dose of electromagnetic radiation between about 1 kGy and about 50 kGy.

49. The method according to claim 39, wherein the electromagnetic radiation is gamma irradiation, and the live virus is subjected to a dose of electromagnetic radiation between about 5 kGy and about 20 kGy.

50. The method according to any one of claims 33-49, wherein the live virus is subjected to the RNA damaging agent at a temperature of 37°C or lower.

51. The method according to any one of claims 44-47, wherein the live virus is subjected to the RNA damaging agent at a temperature of about 25°C.

52. The method according to claim 48 or 49, wherein the live virus is subjected to the RNA damaging agent at a temperature of about -80°C.

53. The method according to any one of claims 33-38, wherein subjecting the live virus to an RNA damaging agent comprises exposing the live virus to an RNA damaging chemical agent.

54. The method according to claim 53, wherein the RNA damaging chemical agent is an alkylating agent capable of crosslinking RNA.

55. The method according to claim 53, wherein the RNA damaging chemical agent is busulfan, cyclophosphamide, melphalan, formaldehyde, carbodiimide or bissulfosuccinimidyl suberate.

56. The method according to claim 53, wherein the RNA damaging chemical agent is a free radical forming agent capable of cleaving RNA.

57. The method according to claim 56 wherein the free radical forming agent is a peroxide, hydrogen bromine, ammonium persulfate, or a hydroxyl radical.

58. The method according to any one of claims 33-57 wherein separating the live virus from a UV-absorbing compound comprises fractionating, in a sucrose gradient, a growth medium containing the live virus.

59. A method comprising:

administering non-replicating virus-derived particles according to any one of claims 1 to 32 to a population of cells in a patient, wherein the population of cells comprises cancerous cells and non-cancerous cells and the administration induces expression and release of cytokines in the patient.

60. The method according to claim 59 wherein the cytokines released in the patient include: interleukins, interferons, inflammatory cytokines, members of the CXC chemokine family, members of the tumor necrosis factor family, or any combination thereof.

61. A method of inducing cell death of cancerous cells in a patient, the method comprising:

administering non-replicating virus-derived particles according to any one of claims 1 to 32 to the patient.

62. A method comprising:

administering non-replicating virus-derived particles according to any one of claims 1 to 32 to a population of cells in a patient, wherein the population of cells comprises cancerous cells and non-cancerous cells and the administration results in preferential cell death of the cancerous cells over the non-cancerous cells.

63. The method according to claim 61 or 62, wherein the cell death is through apoptosis.

64. The method according to claim 61, 62 or 63, wherein the cell death is by innate immune effector cells, adaptive immune effector cells, or both.

65. The method according to claim 64, wherein the adaptive immune effector cells are T-cells, B-cells, or both.

66. The method according to claim 65, wherein the innate immune effector cells are mast cells, phagocytes, basophils, eosinophils, natural killer cells, γδ T cells, or any combination thereof.

67. The method according to claim 66, wherein the phagocytes are macrophages, neutrophils, dendridic cells, or any combination thereof.

68. The method according to any one of claims 59-67, wherein 1E10 to 1E15 non-replicating virus-derived particles are administered to the patient.

69. The method according to any one of claims 59-67, wherein 1E11 to 1E13 non-replicating virus-derived particles are administered to the patient.

70. The method according to any one of claims 59-69 wherein the method further comprises administering a chemotherapeutic to the patient.

71. The method according to claim 70 wherein the chemotherapeutic is bendamustine, dexamethasone, doxorubicin, vincristine, idarubicin, carfilzomib, suberoylanilide hydroxamic acid, melphlan, or the SMAC mimetic LCL161.

72. The method according to claim 72 wherein the chemotherapeutic is bendamustine, busulfan, carboplatin, carmustine, chlorambucil, cisplatin, cyclophosphamide, dacarbazine, lomustine, melphalan, temozolomide, thiotepa, oxaliplatin, procarbazine, pentostatin, cladribine, clofarabine, cytarabine, fludarabine, gemcitabine, hydroxyurea, mercaptopurine, nelarabine, fluorouracil, bleomycin, dactinomycin, daunorubicin, doxorubicin, doxorubicin liposomal, idarubicin, mitoxantrone, capecitabine, topotecan, irinotecan, etoposide, paclitaxel, teniposide, thioguanine, omacetaxin, altretamine, asparaginase, asparaginase, pegaspargase, Isotretinoin, retinoic acid, arsenic, vinblastine, vincristine, vincristine

liposomal, bosutinib, dasatinib, imatinib, nilotinib, sunitinib, vemurafenib, regorafenib, bortezomib, carfilzomib, thalidomide, lenalidomide, pomalidomide, methotrexate, pralatrexate, everolimus, Temsirolimus, vorinostat, romidepsin, valproic acid, decitabine, azacitidine, anagrelide, cortisone, dexamethasone, prednisone, triamcinolone, interferon alfa 2a, interferon alfa 2b, peginterferon alfa 2b, interferon beta 1b, aldesleukin/IL-2, denileukin diftitox, granulocyte colony stimulating factor, granulocyte macrophage colony stimulating factor, anti-CD20, anti-CD47, anti-CD33, anti-CD38, anti-CD138, anti-CS1, anti-CD52, anti-VEGF, anti-Her2/Neu, anti-EGFR, anti-CTLA4 or anti-IGF-1.

73. The method according to any one of claims 59-72 wherein the cancer is leukemia, lymphoma, multiple myeloma, renal cancer, breast cancer, colon cancer, or glioblastoma.

74. The method according to any one of claims 59-72 wherein the cancer is hepatocellular carcinoma, prostate cancer, lung cancer, mesothelioma, uterine cancer, cervical cancer, bladder cancer, ovarian cancer, pancreatic cancer, melanoma, basal cell carcinoma, melanoma, squamous cell carcinoma, esophageal cancer, gastric cancer, osteosarcoma, chondrosarcoma, a soft tissue cancer, head cancer, neck cancer, thyroid cancer, retinoblastoma, or oral cancer.

75. The method according to any one of claims 59-74, wherein the non-replicating virus-derived particles are administered to the patient intratumorally, intranasally, intramuscularly, intradermally, intraperitoneally, intra-arterially, intravenously, subcutaneously or intracranially.

WHAT IS CLAIMED IS

1. A product comprising a non-replicating, cell-internalizing Rhabdovirus-derived particle for treating cancer cells in a subject, wherein said Rhabdovirus-derived particle exhibits RNA which is cross-linked or cleaved into at least two discontinuous RNA polynucleotide sequences.

2. The product of claim 1, wherein said Rhabdovirus-derived particle exhibits:

RNA cross-linked to other RNA nucleotides, to amino acids in a protein structure around the RNA of the Rhabdovirus, or;

the protein structure around the RNA is cross-linked to another protein of the protein structure, or to another amino acid of the same protein;

or both.

3. The product of claim 1, wherein said RNA comprises at least 0.05% cross-linked nucleotides.

4. The product of claim 1, wherein said non-replicating, cell-internalizing Rhabdovirus-derived particle exhibits at least 60 G proteins per particle

5. The product of claim 1 for treating cancer cells, wherein said product is for use in combination with a second pharmacological agent.

6. The product of claim 1, produced by the method of subjecting live Rhabdovirus to an RNA damaging agent to under conditions to cross-link RNA of the Rhabdovirus, cleave the RNA structure of the Rhabdovirus or both.

7. A method of treating cancer in a subject comprising, administering the product of claim 1 to a subject in need thereof.

8. The method of claim 7 wherein about $1x10^{10}$ to about $1x10^{15}$ Rhabdovirus-derived particles are administered to the subject.

9. The method of claim 7, further comprising administering a second pharmaceutical agent to the subject.

10. The method of claim 9 wherein the pharmaceutical agent is a chemotherapeutic agent.

11. A method for producing the product as defined in claim 1 comprising the step of:

subjecting live Rhabdovirus to an RNA damaging agent under conditions to cross-link RNA of the Rhabdovirus, cleave the RNA structure of the Rhabdovirus or both to produce non-replicating, cell-internalizing Rhabdovirus-derived particles.

12. The method of claim 11, wherein the RNA damaging agent is electromagnetic radiation, a chemical cross-linking agent or both.

13. The method of claim 11, wherein the electromagnetic radiation has a wavelength less that about 1mm.

14. The method of claim 12, wherein the RNA damaging agent is electromagnetic radiation with a dose of between about 100 mJ/cm^2 and about 8000 mJ/cm^2 or gamma irradiation with a dose of between 1kGy and about 50kGy.