CLAIMS

What is claimed is:

1. A chimeric oncolytic virus, comprising:

a herpesvirus having a modified nucleic acid sequence, comprising:

a modification of the herpesvirus gamma (1)34.5 gene ($\gamma_1$34.5) or a nucleic acid with at least about 70% homology to the $\gamma_1$34.5 gene that reduces its expression;

a second viral nucleic acid sequence encoding a PKR evasion protein ~~that does not cause virulence~~ is a cytomegalovirus (CMV) nucleic acid and an associated promoter; and

a third nucleic acid sequence encoding a tumor-associated antigen; wherein the tumor-associated antigen includes a secreted protein, a dendritic cell-binding peptide, a glioblastoma-associated antigen, or a full-length EphA2.

2. The chimeric oncolytic virus of claim 1, wherein the herpesvirus is an α herpesvirus.

3. The chimeric oncolytic virus of claim 1, wherein the herpesvirus is an HSV-1 herpesvirus.

4. The chimeric oncolytic virus of claim 1, wherein the modification of the herpesvirus $\gamma_1$34.5 gene comprises a deletion or mutation of the $\gamma_1$34.5 gene.

~~5. The chimeric oncolytic virus of claim 1, wherein the second viral nucleic acid sequence is a cytomegalovirus (CMV) nucleic acid.~~

~~6~~5. The chimeric oncolytic virus of claim 1, wherein the CMV nucleic acid comprises an IRS-1 gene or a nucleic acid having at least 70% homology to the IRS-1 gene.

~~7~~6. The chimeric oncolytic virus of claim 1, wherein the tumor-associated antigen includes a dendritic cell-binding peptide.

~~8~~7. The chimeric oncolytic virus of claim 1, wherein the tumor-associated antigen is a secreted protein.

~~9~~8. The chimeric oncolytic virus of claim 1, wherein the tumor-associated antigen includes a glioblastoma-associated antigen.

~~10~~9. The chimeric oncolytic virus of claim 1, wherein the tumor-associated antigen is EphA2.

~~11~~10. The chimeric oncolytic virus of claim 1, wherein the third nucleic acid sequence is inserted into the chimeric oncolytic virus at the γ134.5 locus.

~~12~~11. The chimeric oncolytic virus of claim 1, wherein the herpesvirus includes a fourth nucleic acid sequence encoding a different tumor-associated antigen from that encoded by the third nucleic acid sequence.

~~13. A method of treating cancer by in a subject by contacting a cancer cell of the subject with a chimeric oncolytic virus, comprising:~~
~~a herpesvirus having a modified nucleic acid sequence, comprising:~~
~~a modification of the herpesvirus gamma (1)34.5 gene ($\gamma_1$34.5) or a nucleic acid with at least about 70% homology to the $\gamma_1$34.5 gene that reduces its expression;~~
~~a second viral nucleic acid sequence encoding a PKR evasion protein that does not cause virulence; and~~
~~a third nucleic acid sequence encoding a tumor-associated antigen.~~

~~14. The method of claim 13, wherein the herpesvirus is an HSV-1 herpesvirus.~~

~~15. The method of claim 13, wherein the modification of the herpesvirus $\gamma_1$34.5 gene comprises a deletion or mutation of the $\gamma_1$34.5 gene.~~

~~16. The method of claim 13, wherein the cancer is selected from the group consisting of adenocarcinoma, hepatoblastoma, sarcoma, glioma, glioblastoma, neuroblastoma,~~

~~plasmacytoma, histiocytoma, melanoma, adenoma, myeloma, bladder cancer, brain cancer, squamous cell carcinoma of the head and neck, ovarian cancer, skin cancer, liver cancer, lung cancer, colon cancer, cervical cancer, breast cancer, renal cancer, esophageal carcinoma, head and neck carcinoma, testicular cancer, colorectal cancer, prostatic cancer, and pancreatic cancer cell.~~

~~17. The method of claim 13, wherein the cancer is glioblastoma.~~

~~18. The method of claim 13, wherein the cancer cell is contacted *ex vivo*.~~

~~19. The method of claim 13, wherein the cancer cell is contacted *in vivo*.~~

~~20. The method of claim 19, wherein the chimeric oncolytic virus is administered in a pharmaceutically acceptable carrier.~~

~~21. The method of claim 16, further comprising administering chemotherapy or radiation therapy to the subject.~~

~~22. The method of claim 16, wherein the tumor-associated antigen is one found on the cancer being treated.~~

~~23. The method of claim 16, wherein tumor-associated antigen is EphA2.~~

~~24. The method of claim 16, wherein the herpesvirus is an HSV-1 herpesvirus.~~

~~25. The method of claim 16, wherein the second viral nucleic acid sequence is a cytomegalovirus (CMV) nucleic acid.~~

~~26. The method of claim 16, wherein the herpesvirus includes a fourth nucleic acid sequence encoding a different tumor-associated antigen from that encoded by the third nucleic acid sequence.~~

27. The method of claim 16, wherein the chimeric oncolytic virus provides a persistent antitumor effect.

28. A method of immunizing a subject against cancer, comprising administering to the subject a chimeric oncolytic virus, comprising:
a herpesvirus having a modified nucleic acid sequence, comprising:

a modification of the herpesvirus gamma (1)34.5 gene ($\gamma_1$34.5) or a nucleic acid with at least about 70% homology to the $\gamma_1$34.5 gene that reduces its expression;

a second viral nucleic acid sequence encoding a PKR evasion protein that does not cause virulence; and

a third nucleic acid sequence encoding a tumor-associated antigen
wherein the chimeric oncolytic virus is administered under conditions effective to immunize the subject against cancer.

29. The method of claim 28, wherein the herpesvirus is an HSV-1 herpesvirus.

30. The method of claim 28, wherein the modification of the herpesvirus $\gamma_1$34.5 gene comprises a deletion or mutation of the $\gamma_1$34.5 gene.

31. The method of claim 28, wherein the cancer is selected from the group consisting of adenocarcinoma, hepatoblastoma, sarcoma, glioma, glioblastoma, neuroblastoma, plasmacytoma, histiocytoma, melanoma, adenoma, myeloma, bladder cancer, brain cancer, squamous cell carcinoma of the head and neck, ovarian cancer, skin cancer, liver cancer, lung cancer, colon cancer, cervical cancer, breast cancer, renal cancer, esophageal carcinoma, head and neck carcinoma, testicular cancer, colorectal cancer, prostatic cancer, and pancreatic cancer cell.

32. The method of claim 28, wherein the cancer is glioblastoma.