WHAT IS CLAIMED IS:

1. A vector comprising a herpes simplex virus (HSV) genome, wherein the vector comprises an alteration that prevents expression of one or more functional ICP4 and ICP47 proteins.

2. The vector of claim 1, wherein: (a) the functional ICP4 and ICP47 proteins are characterized by the amino acid sequences of SEQ ID NO: 3 and 4 (ICP4) and SEQ ID NO: 5 (ICP47); and/or (b) the HSV genome is an HSV-1 genome.

3. The vector of claim 2, wherein: (a) the HSV genome is a McKrae strain genome; and/or (b) the vector, when administered to a subject, results in one or more of: (i) delayed oncolysis; (ii) increased immunogenicity; and (iii) increased immune activation.

4. The vector of any one of claims 1-3, wherein the vector comprises a nucleic acid sequence encoding one or more therapeutic polypeptides.

5. The vector of claim 4, wherein the therapeutic polypeptide:

(a) targets the stroma of a tumor;

(b) supports T cell survival in a tumor microenvironment;

(c) induces tertiary lymphoid structures (TLS) in a tumor bed; and/or

(d) promotes phagocytic innate immune surveillance.

6. The vector of claim 5, wherein the therapeutic polypeptide targets the stroma of a tumor by degrading an extracellular matrix protein.

7. The vector of claim 6, wherein the therapeutic polypeptide comprises hyaluronidase, MMP-9, or an inhibitor of lysyl oxidase.

8. The vector of claim 5, wherein the therapeutic polypeptide targets the stroma of a tumor by activating local endothelium to increase T cell infiltration.

9. The vector of claim 8, wherein the therapeutic polypeptide comprises a proinflammatory cytokine.

10. The vector of claim 9, wherein the proinflammatory cytokine comprises TNF, IL-1β, IL-6 or IL-18.

11. The vector of claim 5, wherein the therapeutic polypeptide supports T cell survival in the tumor microenvironment by enhancing recruitment of T cells to a site of a tumor.

12. The vector of claim 11, wherein the therapeutic polypeptide comprises CCL19 or CCL21.

13. The vector of claim 5, wherein the therapeutic polypeptide supports T cell survival in the tumor microenvironment by supporting T cell function.

14. The vector of claim 13, wherein the therapeutic polypeptide comprises a T cell trophic factor.

15. The vector of claim 14, wherein the T cell trophic factor is selected from IL-7, IL-12, IL-15, IL-18, and IFNγ.

16. The vector of claim 5, wherein the T cell is a CAR T cell.

17. The vector of claim 16, wherein the therapeutic polypeptide comprises soluble TGFβRII.

18. The vector of claim 16, wherein the therapeutic polypeptide comprises an antigen recognized by the CAR T cell.

19. The vector of claim 18, wherein the antigen recognized by the CAR T cell comprises mesothelin.

20. The vector of claim 19, wherein the therapeutic polypeptide comprises a co-stimulatory molecule.

21. The vector of claim 20, wherein the co-stimulatory molecule is selected from CD40L and OX40L.

22. The vector of claim 5, wherein the therapeutic polypeptide induces tertiary lymphoid structures (TLS) in a tumor bed.

23. The vector of claim 22, wherein the therapeutic polypeptide comprises CCL19, lymphotoxin β, CXCL13, or TNF.

24. The vector of claim 5, wherein the therapeutic polypeptide promotes phagocytic innate immune surveillance.

25. The vector of claim 24, wherein the therapeutic polypeptide disrupts the Sirpα/CD47 axis.

26. The vector of claim 25, wherein the therapeutic polypeptide comprises a Sirpα-IgG fusion transgene.

27. The vector of claim 5, wherein the therapeutic polypeptide supports anti-tumor macrophage polarization.

28. The vector of claim 27, wherein the therapeutic polypeptide that supports anti-tumor macrophage polarization comprises TNF, IL-1, IL-12, IL-17, or IFNγ.

29. A method of expressing a polypeptide in a subject comprising administering to the subject the vector of any one of claims 1-28.

30. A method of preparing the vector of any one of claims 1-28, the method comprising incubating cells transfected with:

(a) a first nucleic acid molecule comprising: (i) a portion of HSV genome but does not encode functional ICP4 and ICP47 proteins; and (ii) a sequence that encodes a marker element, wherein the sequence that encodes the marker element is flanked by a first homology region (HR1) and a second homology region (HR2); and (b) a second nucleic acid molecule comprising a sequence that encodes a therapeutic polypeptide, wherein the sequence encoding the therapeutic polypeptide is flanked by a first homology region (HR1) and a second homology region (HR2), wherein HR1 is homologous to HR1 and HR2 is homologous to HR2 such that the sequence encoding the therapeutic polypeptide is integrated into the first nucleic acid molecule via homologous recombination.

31. The method of claim 30, wherein the cells are ICP4 and/or ICP47 complementing cells and/or further comprising a step of purifying viral plaques that do not express the marker element.

32. A variant HSV strain comprising the vector of any of claims 1-28.

33. A cell transduced with a vector of any of claims 1-28.

34. A pharmaceutical composition comprising a vector of any of claims 1-28 and a pharmaceutically acceptable carrier.

35. Use of a therapeutically effective amount of the vector of any one of claims 1-28 in the manufacture of a medicament for reducing the size of a tumor in a subject in need thereof, wherein a therapeutically effective amount of the vector is to be administered to the subject in need thereof to reduce the size of the tumor, and wherein the vector comprises a nucleic acid encoding a therapeutic polypeptide that functions to reduce the size of the tumor.

36. A vector comprising a herpes simplex virus (HSV) genome, wherein the vector comprises an alteration that prevents expression of one or more functional ICP4 and ICP47 proteins, and wherein the vector encodes one or more therapeutic polypeptides that support NK cell survival in a tumor microenvironment (TME).

37. The vector of claim 36, wherein: (a) the NK cell is a native NK cell or a CAR NK cell; (b) the one or more therapeutic polypeptides includes an NK cell recruitment factor; (c) the one or more therapeutic polypeptides includes an NK cell trophic factor; and/or (d) the one or more therapeutic polypeptides includes soluble TGFβRII.

38. The vector of claim 37, wherein: (a) the NK cell recruitment factor is a chemokine ligand; and/or (b) the NK cell trophic factor is selected from IL-2, IL- 15, IL-18, and IFNα.

39. The vector of claim 38, wherein the chemokine ligand is selected from CCL2, CX3CL1, CXCL16, CCL5, CXCL9, CXCL10, and CXCL11.

40. The vector of any one of claims 1-28, for use in therapy.