CLAIMS

1. An oncolytic virus encoding a human recombinant transforming growth factor (TGF)-β2 monomer, wherein the human TGF-β2 monomer comprises:

a cysteine to serine or a cysteine to arginine substitution at an amino acid residue corresponding to residue 77 of human TGF-β2 set forth as SEQ ID NO: 2;

a deletion of the α3 helix corresponding to amino acid residues 52-71 of human TGF-β2 set forth as SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 25 of SEQ ID NO: 2;

an arginine to lysine substitution at an amino acid residue corresponding to residue 26 of SEQ ID NO: 2;

a leucine to arginine substitution at an amino acid residue corresponding to residue 51 of SEQ ID NO: 2;

an alanine to lysine substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 2;

a leucine to valine substitution at an amino acid residue corresponding to residue 89 of SEQ ID NO: 2;

an isoleucine to valine substitution at an amino acid residue corresponding to residue 92 of SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 94 of SEQ ID NO: 2;

a threonine to lysine substitution at an amino acid residue corresponding to residue 95 of SEQ ID NO: 2; and

an isoleucine to valine substitution at an amino acid residue corresponding to residue 98 of SEQ ID NO: 2.

2. An oncolytic virus encoding a human recombinant transforming growth factor (TGF)-β monomer, wherein the human TGF-β2 monomer comprises:

a leucine to arginine substitution at an amino acid residue corresponding to residue 51 of SEQ ID NO: 2;

an alanine to lysine substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 2;

a cysteine to serine or a cysteine to arginine substitution at an amino acid residue corresponding to residue 77 of human TGF-β2 set forth as SEQ ID NO: 2; and

a deletion of the α3 helix corresponding to amino acid residues 52-71 of human TGF-β2 set forth as SEQ ID NO: 2.

3. The oncolytic virus of claim 2, wherein the TGF-β monomer is a human TGF-β2 monomer.

4. The oncolytic virus of claim 2, wherein the human TGF-β2 monomer further comprises at least one amino acid substitution that increases affinity of the monomer for TGF-β receptor II (TβRII).

5. The oncolytic virus of claim 4, wherein the at least one amino acid substitution that increases affinity of the monomer for TβRII comprises:

a lysine to arginine substitution at an amino acid residue corresponding to residue 25 of SEQ ID NO: 2;

an arginine to lysine substitution at an amino acid residue corresponding to residue 26 of SEQ ID NO: 2;

a leucine to valine substitution at an amino acid residue corresponding to residue 89 of SEQ ID NO: 2;

an isoleucine to valine substitution at an amino acid residue corresponding to residue 92 of SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 94 of SEQ ID NO: 2;

a threonine to lysine substitution at an amino acid residue corresponding to residue 95 of SEQ ID NO: 2; and/or

an isoleucine to valine substitution at an amino acid residue corresponding to residue 98 of SEQ ID NO: 2.

6. The oncolytic virus of claim 1, wherein the human TGF-β2 monomer comprises:

a cysteine to serine substitution at an amino acid residue corresponding to residue 77 of human TGF-β2 set forth as SEQ ID NO: 2;

a deletion of the α3 helix corresponding to amino acid residues 52-71 of human TGF-β2 set forth as SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 25 of SEQ ID NO: 2;

an arginine to lysine substitution at an amino acid residue corresponding to residue 26 of SEQ ID NO: 2;

a leucine to arginine substitution at an amino acid residue corresponding to residue 51 of SEQ ID NO: 2;

an alanine to lysine substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 2;

a leucine to valine substitution at an amino acid residue corresponding to residue 89 of SEQ ID NO: 2;

an isoleucine to valine substitution at an amino acid residue corresponding to residue 92 of SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 94 of SEQ ID NO: 2;

a threonine to lysine substitution at an amino acid residue corresponding to residue 95 of SEQ ID NO: 2; and

an isoleucine to valine substitution at an amino acid residue corresponding to residue 98 of SEQ ID NO: 2.

7. The oncolytic virus of claim 6, wherein the amino acid sequence of the human TGF-β2 monomer comprises or consists of SEQ ID NO: 7.

8. The oncolytic virus of claim 1, wherein the human TGF-β2 monomer comprises or further comprises at least one amino acid substitution that reduces aggregation and/or improves folding of the monomer.

9. The oncolytic virus of claim 8, wherein the human TGF-β2 monomer comprises:

a cysteine to valine substitution at an amino acid residue corresponding to residue 7 of SEQ ID NO: 2;

a cysteine to alanine substitution at an amino acid residue corresponding to residue 16 of SEQ ID NO: 2;

a cysteine to arginine substitution at an amino acid residue corresponding to residue 77 of SEQ ID NO: 2; and/or

a valine to arginine substitution at an amino acid residue corresponding to residue 79 of SEQ ID NO: 2.

10. The oncolytic virus of claim 9, wherein the human TGF-β2 monomer comprises:

a deletion of the α3 helix corresponding to amino acid residues 52-71 of human TGF-β2 set forth as SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 25 of SEQ ID NO: 2;

an arginine to lysine substitution at an amino acid residue corresponding to residue 26 of SEQ ID NO: 2;

a leucine to arginine substitution at an amino acid residue corresponding to residue 51 of SEQ ID NO: 2;

an alanine to lysine substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 2;

a cysteine to arginine substitution at an amino acid residue corresponding to residue 77 of SEQ ID NO: 2;

a valine to arginine substitution at an amino acid residues corresponding to residue 79 of SEQ ID NO: 2;

a leucine to valine substitution at an amino acid residue corresponding to residue 89 of SEQ ID NO: 2;

an isoleucine to valine substitution at an amino acid residue corresponding to residue 92 of SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 94 of SEQ ID NO: 2;

a threonine to lysine substitution at an amino acid residue corresponding to residue 95 of SEQ ID NO: 2; and

an isoleucine to valine substitution at an amino acid residue corresponding to residue 98 of SEQ ID NO: 2.

11. The oncolytic virus of claim 10, wherein the amino acid sequence of the human TGF-β2 monomer comprises or consists of SEQ ID NO: 9.

12. The oncolytic virus of claim 9, wherein the human TGF-β2 monomer comprises:

a cysteine to serine substitution at an amino acid residue corresponding to residue 77 of SEQ ID NO: 2;

a deletion of the α3 helix corresponding to amino acid residues 52-71 of human TGF-β2 set forth as SEQ ID NO: 2;

a cysteine to valine substitution at an amino acid residue corresponding to residue 7 of SEQ ID NO: 2;

a cysteine to alanine substitution at an amino acid residue corresponding to residue 16 of SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 25 of SEQ ID NO: 2;

a leucine to arginine substitution at an amino acid residue corresponding to residue 51 of SEQ ID NO: 2;

an alanine to lysine substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 2; and

a lysine to arginine substitution at an amino acid residue corresponding to residue 94 of SEQ ID NO: 2.

13. The oncolytic virus of claim 12, wherein the amino acid sequence of the human TGF-β2 monomer comprises or consists of SEQ ID NO: 10.

14. The oncolytic virus of claim 9, wherein the human TGF-β2 monomer comprises:

a deletion of the α3 helix corresponding to amino acid residues 52-71 of human TGF-β2 set forth as SEQ ID NO: 2;

a cysteine to valine substitution at an amino acid residue corresponding to residue 7 of SEQ ID NO: 2;

a cysteine to alanine substitution at an amino acid residue corresponding to residue 16 of SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 25 of SEQ ID NO: 2;

an arginine to lysine substitution at an amino acid residue corresponding to residue 26 of SEQ ID NO: 2;

a leucine to arginine substitution at an amino acid residue corresponding to residue 51 of SEQ ID NO: 2;

an alanine to lysine substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 2;

a cysteine to arginine substitution at an amino acid residue corresponding to residue 77 of SEQ ID NO: 2;

a valine to arginine substitution at an amino acid residues corresponding to residue 79 of SEQ ID NO: 2;

a leucine to valine substitution at an amino acid residue corresponding to residue 89 of SEQ ID NO: 2;

an isoleucine to valine substitution at an amino acid residue corresponding to residue 92 of SEQ ID NO: 2;

a lysine to arginine substitution at an amino acid residue corresponding to residue 94 of SEQ ID NO: 2;

a threonine to lysine substitution at an amino acid residue corresponding to residue 95 of SEQ ID NO: 2; and

an isoleucine to valine substitution at an amino acid residue corresponding to residue 98 of SEQ ID NO: 2.

15. The oncolytic virus of claim 13, wherein the amino acid sequence of the human TGF-β2 monomer comprises or consists of SEQ ID NO: 12.

16. An oncolytic virus encoding a human recombinant transforming growth factor (TGF)-β2 monomer, wherein the amino acid sequence of the TGF-β2 monomer comprises or consists of SEQ ID NO: 11.

17. The oncolytic virus of claim 2, wherein the TGF-β monomer is a human TGF-β1 monomer.

18. The oncolytic virus of claim 17, wherein the human TGF-β1 monomer further comprises:

an isoleucine to arginine substitution at an amino acid residue corresponding to residue 52 of SEQ ID NO: 1;

an alanine to lysine substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 1;

an alanine to serine substitution at an amino acid residue corresponding to residue 75 of SEQ ID NO: 1; or

an isoleucine to arginine substitution at an amino acid residue corresponding to residue 52, an alanine to lysine substitution at an amino acid residue corresponding to residue 74 and an alanine to serine substitution at an amino acid residue corresponding to residue 75 of SEQ ID NO: 1.

19. The oncolytic virus of claim 18, wherein the amino acid sequence of the human TGF-β1 monomer comprises or consists of SEQ ID NO: 4.

20. The oncolytic virus of claim 2, wherein the TGF-β monomer is a human TGF-β3 monomer.

21. The oncolytic virus of claim 20, wherein the human TGF-β3 monomer further comprises:

a leucine to glutamate substitution at an amino acid residue corresponding to residue 51 of SEQ ID NO: 3;

an alanine to glutamate substitution at an amino acid residue corresponding to residue 72 of SEQ ID NO: 3;

an alanine to aspartate substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 3; or

a leucine to glutamate substitution at an amino acid residue corresponding to residue 51, an alanine to glutamate substitution at an amino acid residue corresponding to residue 72 and an alanine to aspartate substitution at an amino acid residue corresponding to residue 74 of SEQ ID NO: 3.

22. The oncolytic virus of claim 21, wherein the amino acid sequence of the human TGF-β3 monomer comprises or consists of SEQ ID NO: 6.

23. The oncolytic virus of claim 1, wherein the TGF-β monomer further comprises a signal sequence.

24. The oncolytic virus of claim 23, wherein the signal sequence is an IL-2 signal sequence comprising the amino acid sequence of SEQ ID NO: 8.

25. The oncolytic virus of claim 1, wherein the virus is a vaccinia virus, a herpes simplex virus, or an adenovirus.

26. The oncolytic virus of claim 1, wherein the virus is a vaccinia virus.

27. The oncolytic virus of claim 26, wherein the vaccinia virus comprises a modification of the gene encoding thymidine kinase (TK) and a modification of the gene encoding virus growth factor (VGF).

28. The oncolytic virus of claim 27, wherein the modification of the gene encoding TK comprises a complete or partial deletion of the gene.

29. The oncolytic virus of claim 28, wherein at least a portion of the TK gene is replaced with a nucleic acid encoding the TGF-β monomer.

30. The oncolytic virus of claim 27, wherein the modification of the gene encoding VGF comprises a complete or partial deletion of the gene.

31. A composition comprising the oncolytic virus of claim 1 and a pharmaceutically acceptable carrier.

32. Use of the composition of claim 31 in the manufacture of a medicament for the treatment of cancer, or for inhibiting tumor growth or tumor metastasis in a subject with cancer.

33. The method of claim 32, wherein the cancer is melanoma, head and neck cancer, or pancreatic cancer.

34. The composition of claim 31 for use in therapy.