WHAT IS CLAIMED IS:

1. An oncolytic vaccinia virus comprising a nucleic acid encoding a Toll/IL-1R domain-containing adapter inducing interferon beta (TRIF) protein or a functional domain thereof.

2. The oncolytic vaccinia virus of claim 1, further comprising one or more of the following modifications:

(i) a viral backbone mutation;

(ii) an envelope with reduced glycosylation relative to an unmodified virus;

(iii) incorporation of a nucleic acid that encodes granulocyte-macrophage colony stimulating factor (GM-CSF), IL-12, IFN-γ, IL-18 or a combination thereof;

(iv) incorporation of a nucleic acid that encodes a prostaglandin E2 (PGE2) antagonist, incorporation of a nucleic acid that encodes 15-PGDH or a combination thereof; and/or

(v) a mutation selected from the group consisting of an A34R Lys151 to Glu mutation, complete or partial deletion of B5R, a mutation or deletion of A36R, a mutation or deletion of A56R and a combination thereof.

3. The oncolytic vaccinia virus of claim 2, wherein the viral backbone mutation is a B8R deletion, a B18R deletion, an A35R deletion, or a combination thereof.

4. The oncolytic vaccinia virus of claim 2 or 3, wherein the oncolytic virus is modified by the incorporation of a nucleic acid encoding GM-CSF.

5. The oncolytic vaccinia virus of claim 2, 3 or 4, wherein the oncolytic virus is modified by the incorporation of a nucleic acid encoding a prostaglandin E2 antagonist.

6. The oncolytic vaccinia virus of claim 2, 3, 4 or 5, wherein the oncolytic virus is modified by the incorporation of a nucleic acid encoding 15-PGDH.

7. The oncolytic vaccinia virus of claim 2, 3, 4, 5 or 6, wherein the viral backbone mutation is a deletion or functional deletion of C12L.

8. The oncolytic vaccinia virus of claim 2, 3, 4, 5, 6 or 7, wherein the oncolytic virus is thymidine kinase (TK) negative.

9. An oncolytic vaccinia virus comprising:

(i) a Thymidine kinase (TK) deletion;

(ii) an envelope with reduced glycosylation (*e.g.*, reduced sialylation) relative to an unmodified virus; and

(iii) a nucleic acid encoding TRIF, or a functional domain thereof.

10. An oncolytic vaccinia virus comprising:

(i) a Thymidine kinase (TK) deletion;

(ii) an envelope with reduced glycosylation (*e.g.*, reduced sialylation) relative to an unmodified virus;

(iii) a nucleic acid encoding TRIF, or a functional domain thereof; and

(iv) a nucleic acid encoding 15-PGDH, or a functional domain thereof.

11. An oncolytic vaccinia virus comprising:

(i) a Thymidine kinase (TK) deletion;

(ii) an envelope with reduced glycosylation (*e.g.*, reduced sialylation) relative to an unmodified virus;

(iii) a nucleic acid encoding TRIF, or a functional domain thereof;

(iv) a nucleic acid encoding 15-PGDH, or a functional domain thereof; and

(v) a C12L deletion.

12. An oncolytic vaccinia virus comprising:

(i) a Thymidine kinase (TK) deletion;

(ii) an envelope with reduced glycosylation relative to an unmodified virus;

(iii) a nucleic acid encoding TRIF, or a functional domain thereof;

(iv) a nucleic acid encoding 15-PGDH, or a functional domain thereof;

(v) a C12L deletion; and

(vi) a B5R deletion.

13. Use of the oncolytic vaccinia virus of any one of claims 1-12 for the manufacture of a medicament for reducing the growth of a cancer cell.

14. Use of the oncolytic vaccinia virus of any one of claims 1-12 for the manufacture of a medicament for reducing the growth of a tumor.

15. Use of the oncolytic vaccinia virus of any one of claims 1-12 for the manufacture of a medicament for treating a subject having a cancer.

16. Use of the oncolytic vaccinia virus of any one of claims 1-12 for the manufacture of a medicament for producing an anti-cancer effect in a subject.

17. The use of the oncolytic vaccinia virus of any one of claim 13-16, wherein the medicament further comprises one or more agents selected from the group consisting of an anti-cancer agent, an immunomodulatory agent, and a combination thereof.

18. An oncolytic vaccinia virus of any of the preceding claims 1-12, for use in the treatment of cancer in a subject.